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Vol. 122, No. 3
September 1955

The Journal of
NERVOUS AND MENTAL DISEASE

An Educational Journal of Neuropsychiatry, founded in 1874

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Published monthly by
THE WILLIAMS & WILKINS COMPANY
BALTIMORE 2, MARYLAND

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The Journal of
Nervous and Mental Disease

Vol. 122, No. 3 SEPTEMBER 1955 Serial No. 885

CLINICAL REACTIONS AND TOLERANCE TO LSD IN CHRONIC SCHIZOPHRENIA

LOUIS S. CHOLDEN, M.D.,[1] ALBERT KURLAND, M.D.,[2] AND
CHARLES SAVAGE, M.D.[1]

HISTORICAL REVIEW

Since Hofmann's (15) description in 1943 of the altered state of consciousness produced by LSD, a number of attempts have been made to elucidate the relationship between LSD and psychotic reactions. Because the LSD state manifests many of the characteristics of the schizophrenic reactions, considerable emphasis has been placed on comparing and evaluating this similarity. The experimental value of a drug which could produce a controlled schizophrenic state would be inestimable. It stimulates the imagination to conceive the creation of a model psychosis which can be studied psychodynamically, biochemically and subjectively at once. The hope for an ingress into the mysteries of schizophrenia has resulted in studying this problem from many differing viewpoints.

Some investigators have studied the effect of this drug on the chronic schizophrenic patient. Many of them describe a diminished response in these patients compared with normals. Stoll (15) gave LSD 20 times to six schizophrenics who had proven immune to therapy and found: 1) "the effects were relatively sparse and less colorful than in normal subjects"; 2) relatively higher doses were required to produce an effect; 3) the reaction of one patient to 100 μg. was much weaker the second time he received it than the first time; 4) there was no doubt as to which were functional and which were toxic symptoms. He concluded that in view of the very small doses required, LSD might be considered a trace element in the development of endogenous psychoses. He mentioned the possibility that the weaker reactivity might be either immunity to the drug or schizophrenic negativism. Condrau (4) found, in general, 1) that psychotics were more resistant to LSD, 2) that the course of LSD intoxication was blander, and 3) that the disturbances in perception, consciousness and ego feeling were less in the psychotic patients. He also proposed the question that the psychotic patient had a specific immunity to the LSD. He hypothesized that psychoses might be produced by a substance similar to LSD, possibly produced in significant concentrations in the body.

Manfred Bleuler pointed out (2) that LSD was most interesting because of the relatively higher doses required to produce an effect in psychotics than were required by normal subjects. He did not feel that the effect was sufficiently discrete to serve as a diagnostic criterion.

De Giacomo (5) confirmed Condrau's opinion that psychotics are very resistant to LSD. He studied relatively high doses, 300–500 μg. on 12 patients, 9 schizophrenics and 3 oligophrenics, and was able to produce excited catatonic states in non-catatonic patients.

Belsanti (1) in 1952 gave 80–480 μg. of LSD to 14 schizophrenics and 2 oligophrenics. He concluded that LSD has a specific schizogenic action, that it heightens the symptoms in schizophrenics and produces them anew in oligophrenics.

In England Mayer-Gross (11) gave LSD to 13 schizophrenic patients and found that the psychological effects were minimal although his tabulated results show that seven developed euphoria and one showed outbursts of anger.

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Liddell and Weil-Malherbe (10) gave IV LSD to six schizophrenic patients. They observed aggravation of the clinical picture blocking, incoherence, perseveration, echolalia and poor production of material in these patients. They also noted rapid mood swings. Two of the schizophrenic patients gave evidence of visual and auditory hallucinations. They were frightened and completely inaccessible.

Sloan and Doust (14) gave LSD to 7 patients with schizophrenia and found slight although clinically apparent changes due to LSD that were difficult to verify objectively.

In this country Busch and Johnson (3) studied 18 schizophrenic patients and noted the chief effect of LSD to be excitation. These patients moved more, showed greater interest, responded more, talked more, exhibited more emotion, and expressed more psychopathology verbally. Some had short periods of disorientation, confusion and occasional temporary visual hallucinations. Most of them showed euphoria.

Forrer and Goldner (6) gave LSD to 6 schizophrenics who had failed to respond to treatment. Five of the six showed euphoria and increased verbal productivity; all patients showed hallucinations although these could not be determined at the time the patients were under the influence of the drug. Increased sexual material was apparent in three patients.

Hoch, Cattell, and Pennes (7) studied 21 schizophrenic patients and observed mental changes if more than 60 μg. were used. They found perceptual disturbances, including hallucinations and illusions, unreality feelings, disturbance of time sense, disturbances of thought and language process in every patient when the doses exceeded 10 μg. Emotional disturbances were common including anxiety, depression and euphoria. There was an intensification of catatonic and paranoid pictures. They state "the well-preserved pseudoneurotic schizophrenics and the undeteriorated or moderately deteriorated overt schizophrenics showed the more intense over emotional reactions to the drug."

In the group of severely deteriorated schizophrenic patients, the emotional response was at times intense, but often no content was verbalized and gross catatonic withdrawals ensued. Deteriorated schizophrenic patients respond differently than do well-preserved schizophrenic patients.

They commented that "schizophrenic patients whose reality contacts have already been impaired are seemingly more vulnerable to drugs that have a disorganizing effect on reality perceptions."

Pennes (12) gave LSD to 25 schizophrenics and found symptom intensification in 64%, while 24% had a biphasic reaction of normalization and intensification.

Hoch, Cattell and Pennes (7) in comparing schizophrenia with the drug induced psychoses feel that there are differences and that these differences do not permit an analogy to be drawn to the two conditions. This is in contrast to the view of Hoffer, Osmond and Smythies (9) and Rinkel, Hyde, and Solomon (13) who feel that they are analogous.

Hoch (8) states that LSD shows a marked difference of response between acute schizophrenic and deteriorated schizophrenic patients. He says "while acute schizophrenic patients respond with great intensity to LSD and mescaline which reinforce and underscore their symptomatology, most of the deteriorated schizophrenics show very little response to the drug."

PRESENT STUDIES[3]

The first part of the present study was directed at ascertaining what reaction chronic, regressed, schizophrenic patients would show to LSD inasmuch as the results in the literature differed. This was preliminary to a later study designed to assess the possible therapeutic use of this drug. This presentation will describe some methods used for studying the effects of LSD on chronic schizophrenic patients and some of the associated phenomena which were encountered in the course of this study.

METHOD

As far as we could ascertain, LSD has not been previously administered intramuscularly.

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[3] The lysergic acid diethylamide (LSD-25) used in this study was furnished through the courtesy of the Sandoz Chemical Works, Inc. New York.

However, this route seemed preferable for administration to chronic schizophrenic patients. It overcomes the problem of oral administration where negativism might result in failure to swallow all of the drug. Also there would be no question concerning intestinal absorption. Intravenous administration with chronic schizophrenic patients is sometimes difficult to accomplish.

A simple behavior rating scale was assembled which could be completed by relatively uneducated aide personnel. It was essentially a gleaning of items from the many rating scales now in existence, which would highlight behavioral manifestations of psychological state. (table 1).

These observation forms were filled out by each aide in charge of each patient for every shift. An observer whose only task was to fill out the rating scales, saw the patients each evening for 3 hours. The ward psychiatrist and another hospital psychiatrist each saw the patients three times a week. They made clinical notes and filled out Lorr Rating Scales.

The first four female patients who satisfied the following criteria were picked as subjects from a review of their records. They must 1) have been in the State Hospital for 15 years without parole; 2) relatively stable in their symptomatology for the past 5 years; 3) be under the age of 40; 4) be classified as chronic regressed schizophrenic patients; 5) have graduated from grammar school; 6) have spent some time in this ward within the past year without benefit. These patients were transferred to the new ward where they could be better studied and observed.

There was a period of 3 weeks' observation before any injections were given. This was followed by a 3-week period when only placebo was given. Thus it was possible to rate the effects of the change of ward and to assess the effects of the IM needle.

After this time, 100 μg. of LSD were given to 2 patients, and placebo was continued with the other 2 patients. No one in any way associated with these studies, including the investigator, knew which patients were to get the drug and which the placebo. The Sandoz Company had kindly prepared vials of saline to serve as placebos which were identical in appearance with the LSD vials.

This experimental design was not absolutely necessary in the light of the later results, for, on the day the first dose of LSD was given, it seemed clearly evident which 2 of the patients were receiving something new.

CLINICAL REACTIONS

One catatonic patient who had been mute for some years suddenly burst into loud wailing sobs which were shortly followed by overwhelming bursts of laughter starting 35 minutes after the drug was given. This patient seemed most distressed and shaken. Intermittently she would open her mouth as if she were trying desperately to talk or at least to exercise the muscles of her mouth. She also expressed a state of acute anguish with her body movements. When asked why she was crying, she said, "You should never leave the farm." A half hour after the crying started, the wails seemed to end in a giggle. Soon the tears diminished, and she had almost continuous waves of laughing for another hour or so. The patient then began to walk about the ward studying the walls and the windows as though she were seeing them for the first time. She seemed to respond to hallucinations, for she began to talk to non-present individuals. Every few moments for the next few hours she would shake with laughter, and then she might talk a little. Her speech was never particularly coherent, and she soon became preoccupied with the fact that something or somebody was tickling her. She often said she enjoyed things very much and that this was a nice ward, etc.

Three hours after the drug was given, the patient was prancing about the ward and still bursting into gales of laughter. She could hardly eat since she said she had no appetite. That afternoon she played basketball for the first time since she was admitted to the hospital although the opportunity had been offered to her many times. She seemed interested in the effort and was pleased at her attempts. She walked about briskly, smiling broadly, and occasionally laughing. That evening she went to a dance and danced with another patient for the first time. She continued talking until bedtime. The next morning when she awoke, she was her old catatonic self, unable to

TABLE 1.—OBSERVATION CHART FOR WARD PERSONNEL

Name of Patient ____________________ Date ____________

Name of Observer ____________________ Shift ____________

This chart is organized to get your *daily* impression of your patient's behavior. The answers are arranged under the line so you can check the place that best describes the patient's behavior today. Some of the answers will be hard to decide upon. Don't worry about it! Do the best you can; we know it won't be easy. Sometimes the answers will lie between two points on the line. If so, check between the points.

If you don't know the answer, mark (x) in the don't know box in the corner. If you want to, you can write a few words saying why it's hard to answer that question.

At the end of the paper you should mention anything unusual you noticed about the patient.

Also remember, this is a description of how your patient acted *today.*

NOTE: *If you didn't see much of the patient,* mention *it at the end of the chart.*

Each aide should make a chart out for each *of the four patients each day—there are special charts for the night shift.*

Example: Patient who soiled herself 3 or 4 times today, but also went to the toilet.

TIDINESS—TOILET ________ Don't know

		x		
Went to toilet when she had to. No mess	One accident today	Sometimes went to toilet. Sometimes soiled self	Soiled self a lot. Did not attempt to go to toilet	Smeared feces

ACTIVITY ________ Don't know

Didn't move at all	Hardly moved at all	Stayed in one place most of shift	Moved a little, less than average	Was as active as normal person would be	Little overactive	Quite restless and overactive	Hardly rested at all	Always moving around, no stopping her

SPEECH—AMOUNT ________ Don't know

Didn't talk at all	Hardly talked at all. Even when spoken to	Would only talk when spoken to	Kind of quiet. Didn't talk much	Average amount of talking	Kind of talkative	Talked a lot	Talked almost all shift	Talking all the time

MOOD CONTENT ________ Don't know

Extremely depressed and unhappy (or cried a lot)	Very sad or maybe crying	Seemed quite sad or unhappy	A little blue	Pleasant	Overly cheerful	Happy and laughing much more than average	So happy and laughing she bothered others	Wouldn't stop laughing no matter what happened

SPEECH—LOUDNESS ________ Don't know

Could never hear what she said	Often did not hear what she said because she spoke quietly	Spoke very quietly	Occasionally spoke very softly	Normal tone of voice	Raised her voice sometimes	Talked too loudly often	Talked too loud whenever she said anything	Screaming whenever she spoke

TABLE 1.—*Continued*

EATING—DESIRE

______Don't know

Ate anything she saw, including objects on floor	Grabbed to eat anything on table	Asked for 2 or 3 extra helpings	Ate an extra amount	Ate average amount	Ate by herself but needed a little coaxing	Ate very little even with coaxing	Had to be spoon-fed	Had to be tube fed

DESTRUCTIVENESS

______Don't know

Didn't tear anything	Tore a magazine or clothes once	Tore a few things today	Tore many things today	Tore anything she could get her hands on

TIDINESS—CLOTHES

______Don't know
______Didn't get clothes

Dressed neatly	A little messy	Clothes very disorderly	Dressed bizarrely or partially undressed	Completely undressed

TOILET HABITS

______Don't know
______No B.M.

Went to toilet when she had to. No mess	Soiled self once today	Sometimes went to toilet sometimes soiled self	Soiled self a lot. Did not attempt to go to toilet	Smeared feces

SPEECH

______Don't know
______Didn't speak

Always spoke sensibly	Sometimes hard to understand	Often hard to understand	Hardly speaks sensibly all shift	Never spoke sensibly today

SOCIABILITY

______Don't know
______In seclusion

Paid an ordinary amount of attention to others	Paid only a little attention to others	Paid practically no attention to others	Paid no attention to anyone else	Avoided everyone

MOOD—CHANGES

______Don't know

Same mood all day	Slight changes in mood	Occasional mood changes	Often changing mood	Constantly changing moods

TEMPER—CONTROL

______Don't know

Didn't get angry today	Was occasionally angry for some good reason	Flies off the handle with the slightest excuse	Sometimes angry with no excuse, often had temper tantrums	Many temper tantrums. Angry all day long

EATING HABITS

______Don't know

Good eating habits	Used spoon but somewhat sloppy	Used spoon but messy and slobbers	Ate with fingers, bad manners	Ate with fingers, slobbering like an animal

TABLE 1.—*Continued*

COOPERATION ______Don't know

Comes readily when called	Takes her time when answering call	Required calling a number of times	Refused to come when called (Unless seemed she would be forced)	Required force to get her to do anything

EROTICISM ______Don't know

Scratch out item that doesn't apply.

Never see her basturbate or talk about sex	Occasionally she masturbates or talks about sex	Often masturbating or talks about sex	Usually masturbating or talking about sex	Always masturbating or talking about sex

Did you see much of the patient? ______

Did you notice any behavior unusual for this patient? ______

If so, what was it? ______

Did the patient fight today? ______

NIGHT SHIFT

Aides: Please fill this chart at the end of your duty.

AROUSAL ______Don't know

Got up herself before call, or on first call	Awoke when called a couple of times	Needed extra attention to get up	Responded slowly to awakening needed prodding	Very difficult to awaken. Needed a lot of attention

DRESSING ______Don't know

Dressed self	Dressed with a little help	Needed much help to dress	Hard to get her to dress	Impossible to get her dressed

SLEEP—AMOUNT ______Don't know

Slept normal amount of hours	Slept most of night	Slept about half of night	Hardly slept (2 hours)	Didn't sleep at all

SLEEP—PEACEFULNESS ______Don't know

Calm sleep	Rare tossing and turning	Some tossing and turning	Quite a bit of tossing and turning	Always tossing and turning

SLEEP—TALKING ______Don't know

Quiet sleep	Occasional talking	Some talking	Quite a lot of talking	Always talking in sleep

SLEEP—DEPTH ______Don't know

Deep sleep not disturbed	Slept calmly but awakened with noise	Light sleeper	Awoke easily with outside noise	Half asleep and half awake

NIGHT—ACTIVITY ______Don't know

Stayed in bed all night	Got up to walk around once	Got up a few times	Out of bed much of the night	Couldn't get her to stay in bed

TABLE 1.—*Concluded*

NIGHT—TOILET				______Don't know
Did not go to toilet after bedtime	Went to the toilet once during the night	Went to the toilet a few times tonight	Many trips to toilet	Wanted to go to the toilet all night

Note anything unusual, such as—gave sedation (how much) ____________
(any extra) ____________

Wet bed______
Walked in sleep______
Nightmares______
Pleasant dreams______

speak, unable to show interest in anything about her, and quite withdrawn.

On this day the patient received another injection. She laughed a little at first, spoke a few words, but a few hours later lapsed into her previous mute and withdrawn behavior. Thus on the second day we had slight evidence of change from her previous behavior, however, much less than the change observed on the first day the drug was given.

When the patient received the same dosage the third morning, she showed no response at all.

Miss B., the second patient who received LSD, was diagnosed a hebephrenic schizophrenic. She had been in the hospital for 15 years. She commonly stood about the ward with her clothes in bizarre disarray, constantly giggling and laughing about the birds and the flowers in May. However, one-half hour after receiving her first 100 μg. dose of LSD, the silliness and laughter disappeared entirely. She became very serious, and while much of her communication was incoherent and bizarre, there was no giggling or laughter associated with it. In fact, she seemed quite serious. That morning she called her ward doctor by his correct name for the first time. She said "Dr. X, this is serious business—, we are pathetic people—don't play with us."

This is a most unusual type of statement from this patient. The psychiatrist who had been seeing her 3 times a week for the past 6 weeks also had the impression that she was responding to hallucinations. He had never been conscious of this with her before. She looked off into space in a dreamy way and talked to someone out there. She soon was rather seriously calling for help because she was in a very difficult situation. On that day she soiled her dress and tore off her clothes. About 3 hours after the drug was given, Miss B. assaulted the aides and later attempted to embrace and make sexual overtures to the chief nurse. This kind of behavior had never been noted before. On this day she did something characteristic of her only on the days she was reacting to LSD, namely, to get on a chair and hang on the screen of the dayroom. That night the patient kept chattering constantly and even at 1 o'clock in the morning was making and remaking her bed. She was given barbiturates and shortly after this went to sleep.

The next morning she awoke again giggling and silly. About a half hour after 100 μg. of LSD were given, she began talking in the same manner she had the previous day and again hung on the screen. However, this patient also did not show as marked an effect on the second day. On the third day the same dose of drug was given to this patient with no effect. The drug was continued daily for 2 weeks with no noticeable difference in behavior from the observation or placebo period.

The 2 patients who received placebos showed no major changes, either clinically or on the rating scale. They seemed puzzled by the changed behavior of the other patients, but this did not seem to affect their behavior. Later when they received the drug, marked responses were seen. One of these patients who was commonly assaultive and almost constantly in seclusion became calm, friendly and laughed when under the influence of the drug. Of course she would be taken out of seclusion at these times. She wanted to kiss one of the female aides. When she was asked how she was feeling, she often said "I feel crazy."

The other patient who was huddled in the corner nude and masturbating, unable to talk or look at anyone, moving about every few hours, also changed considerably when LSD was given to her. First, she started smiling very broadly, began to pat people on the shoulder, touched them and desired to make some type of quiet contact. Then she put her head in the investigator's lap and indicated that she wanted him to pat her head. This went on for a long time. She would laugh intermittently. On the second day of drug administration, the effect seemed to be diminished. On the third day of LSD administration there seemed to be no response in either of these 2 patients.

Thus, in each of our first four patients we saw a marked change in behavior on the first day of drug administration. It seemed to diminish on the second day the drug was given, and on subsequent administrations was not noticeable. We continued giving the drug in 100 µg. doses for a period of 2 weeks, and no further effect was noted. We therefore felt we were dealing with the phenomenon of tolerance to the drug; tolerance that was manifested on the second daily dose and was complete on the third day of drug administration.

TOLERANCE

It then seemed desirable to study some of the characteristics of this rapidly developing tolerance. It is unusual that tolerance to a drug occurs on the second and is complete on the third dose. Our first attempts were to observe whether the tolerance decreases with a drug-free time interval. After experimentally varying the time interval between drug administration, it was noted that a reaction similar to the strong first reaction to LSD would be shown if approximately 5 days were allowed to elapse between LSD injections. Some patients seemed to show a slight reaction to the drug after a 4-day drug-free interval. However, this was not the same order of reaction that was manifested on the first day. By the fifth day about all showed a strong reaction to the drug. One of our patients, however, showed a somewhat lesser reaction to the drug on the fifth day and a stronger reaction on the sixth day.

Later, in an attempt to overcome the tolerance manifested by these 4 patients the dosage was increased by 100 µg. daily. Thus, each patient would receive 100 µg. the 1st day, 200 µg. the 2nd day, 300 µg. the 3rd day, 400 µg. the 4th day, and 500 µg. the 5th day. The response to this dosage schedule was as follows: The 1st day there was a large response, the 2nd day there was a lesser response, the 3rd day and the 4th day there was no response. A very questionable response was suggested on the 5th day with 500 µg. We did not attempt to give dosages larger than 500 µg. to any of our patients. It might, however, have been possible to overcome the tolerance by using higher dosages.

CROSS-TOLERANCE

In an effort to test the cross-tolerance between the various LSD derivatives, LSD was tested with LAE and brom-lysergic acid. A cross-tolerance was noted in these 3 drugs; that is, the patients who would not respond to LSD because they had developed a tolerance to that drug also did not respond to LAE and brom-lysergic acid. However, it was noted that one of our patients showed a marked gastric upset to LAE, vomiting and manifesting signs of nausea and pain in her stomach, even though she showed none of the psychological manifestations that would indicate the hallucinatory experiences she showed with LAE in the non-tolerant state.

In an effort to test the hypothesis that this tolerance was psychological in nature, a hypothesis that these patients could adjust in this short time to the psychic effects of LSD, an attempt was made to alternate LSD and mescaline. Mescaline hydrochloride rather than mescaline sulfate was used since it was more soluble and more easily prepared for intramuscular administration. The records showed that patients who were tolerant to LSD did not manifest the same tolerance to mescaline. In other words, if they were given LSD on Monday and Tuesday and normally would show no response to LSD on Wednesday, they would be given mescaline on Wednesday instead. They showed their usual response to mescaline at this time. This indicates that tolerance to LSD is not transferred to mescaline HCl, whereas it is transferred to other lysergic acid compounds.

The order and type of behavioral response to LSD and mescaline seemed to be very similar. However, their physiological mechanics must be different insofar as tolerance to LSD does not indicate tolerance to mescaline. If tolerance were the result of psychological encapsulation of the anxiety produced by LSD, would they not show this same encapsulation to a similar psychological upset caused by mescaline? Of course the question of whether the psychic upset is really similar in these two drugs cannot be answered at present. The fact that they did not show this type of cross-tolerance between the two drugs, while there was cross-tolerance between the various LSD derivatives, would suggest, however, that the tolerance has a physiological basis rather than a psychological one. Certainly, our numbers are not large enough to state this with any finality; we simply wish to point out the indications from this limited study.

OTHER CLINICAL REACTIONS

In order to assess the reaction to LSD in other age ranges of hospital population, other groups of patients were studied in a similar manner. A few of the typical clinical reactions were as follows:

Two older male patients were given LSD, Mr. G., age 60, and Mr. K., age 57. Mr. G. responded with wild bursts of laughter which was most unusual for him since Mr. G. never spoke. Mr. K., who stands tensely rigid and uncooperative, seemed to become very flushed, retched a few times and then went to bed. He was occasionally heard to speak at these periods. Later, these patients were given doses of 200 μg. of LSD, and the same reactions and the same tolerance described above were manifested to this dose.

However, it is to be noted that as time went on and these patients were given drugs, they seemed to show a markedly diminishing effect to the drugs even after their tolerance period, despite the larger dose of 200 μg.

Four young males were given this drug, using 100 μg. of LSD. These patients were schizophrenics who had been in the hospital for a few years, and who ranged in age from 22 to 30. Two of these patients responded to the drug by going to sleep on the floor of their noisy ward, something they had not done previously. One of these was a markedly overactive, pacing, agitated patient. The other, a quiet, inhibited, withdrawn young man, seemed to withdraw even further with the administration of LSD.

Another young man, who has usually been aggressive, occasionally assaults aides and doctors, often spits in the doctor's face, began to laugh hilariously 30 minutes after the drug was administered. His explanation for his laughter was that he was so happy. No aggressive outbursts were ever noted while he was responding to LSD.

Some patients were then studied more intensively by daily interviews with a psychiatrist. One patient was a 36-year-old woman who for the four years preceding her admission had the chronic fixed delusion that she was dead and had no body. In addition she was depressed, phobic, and had become increasingly withdrawn and remote. After one month of study, she received 50 μg. of LSD. Initially she complained of giddiness and wanted to lie down but refused to lie down in front of the doctor. She became more hypochondriacal and complained of dying and not having a body. She laughed and said happily, "I shouldn't be laughing."

Later she developed a strong sexual feeling. "It's not stimulating me exactly; it's just that I like you, you know and naturally you want to—I don't know—I'm not very good at anything like this under these circumstances; I'd be better if I had a body and was out in the moonlight with you" (laughs); "I'm hopeless and incurable; hopeless in love and incurable; you're so cute; it's a good thing I don't have a body, I'd really go overboard." She commented this would be wonderful for treating the emotionally ill; it relaxes, yet it stimulates.

This upsurge of libidinal feelings with its associated euphoria was subsequently anxiety provoking, and the anxiety expressed itself in terms of increased somatic preoccupation and complaint, with reinforcement of the delusion of having no body. She then became self-accusatory and depressed, and profound quiet feelings were experienced. She soon re-experienced her reactions during the acute phase of her illness.

SUMMARY

Of the 20 patients who received LSD the following general categories of reaction to LSD were noted:

1. *Covert*—while some patients at first glance show no apparent reaction to LSD,

closer scrutiny often leads to the conclusion that there is a marked albeit subtle effect. *Each* of our subjects showed some unusual behavioral manifestation as a result of the drug administration.

For example, one patient lay in a fetal posture, mute, withdrawn, and staring. After 200 μg. of LSD she continued mute, withdrawn, and staring. She was listed as having no reaction except for pupillary dilation. Subsequently the night nurse reported that she wept bitterly all evening, a mode of reaction foreign to her usual one.

Another patient was described as having no reaction and during the interview situation appeared his usual absent-minded, preoccupied restless self. However, it turned out that this man, who usually tears off his clothes and paces the ward like a panther, had curled up and slept peacefully on the floor for an hour after the LSD took effect. This was an obvious reversal of his usual behavior.

A third patient was at first considered to have no reaction. After 100 μg. of LSD he seemed to remain rigid, mute, withdrawn in a state of waxy catatonia. Yet, actually he too had a reversal. He became preoccupied with the ward activities, dancing frequent, furtive and appealing glances about him instead of keeping his eyes glued shut. In addition, he accepted and smoked a cigarette, something he had not done for four years even though they were offered to him often.

The assessment of LSD effects by objective observation of behavior is more reliable than subjective reports where negativism, withdrawal and denial may lead to the erroneous conclusion that LSD has no effect.

2. *Intensification*—some patients show an intensification of their usual symptomatology and behavior patterns. This may express itself as an intensification of the prevailing mood, increase in anxiety, increase in withdrawal, increased agitation, increased preoccupation with delusion and somatic complaints. Our observations indicate that intensification is more common in the more acute schizophrenic patients. For example: A young lady who was only mildly suspicious became sure people were looking at her through the door, she was being raped, and was much more panic stricken than usual.

A man who was very quiet, bemused and withdrawn lay on the floor and slept in the dayroom with noise all about him when given 100 μg. of LSD.

3. *Reversal*—striking reversals of accustomed behavior often occurred. Patients who were mute became talkative, those who were hyperactive fell asleep, those who were hostile became friendly and warm. Such a reversal may be followed by a subsequent intensification. One of our patients showed a reversal reaction consisting of elation, increased communication, with pleasant sexual fantasies and rather forward behavior followed by intensification of depression and anxiety and phobias, increased somatic complaints and delusion formation, and finally withdrawal.

In a study which will be reported at a later time, 6 patients who had been in a state hospital for from 10 to 20 years, who were under the age of 40, and who were relatively stable in their symptomatology for the past 5 years were taken to the better equipped wards of the Clinical Center of the National Institutes of Health.

These patients were studied closely for a period of 2 months before any LSD was given to them. In the very permissive and understanding environment utilizing an unusually high nursing-patient ratio, considerable change was noted in the patients' behavior. Presumably this was a result of this change milieu during the 2 months of the initial study.

It is interesting to note that these patients, who had been living in the back wards of state hospitals for a number of years, showed this change as a result of the change of physical and social environment. When these patients were given 100 μg. of LSD, there was considerably less behavioral change noted than the changes outlined in the patients reported above. There were no outbursts of laughter in any of the 6; there were fewer marked behavioral changes that were so clearly evident above. These patients were under constant surveillance and were well observed.

The question then arises whether this difference in response is related to the change in environment, or related to the fact that these patients have so recently undergone a major change. Could it be that after having undergone a major change, the patients do not respond so strongly to LSD because change has already been accomplished, or their personalities are already in flux? It is also possible that they felt more comfortable in the acceptance and relative freedom of this friendly environment, and consequently the psychic upset resulting from LSD did not raise as much anxiety and turmoil as with the other patients.

CONCLUSIONS

1. LSD can be given intramuscularly over a protracted period without untoward effects. Consistent results are obtained from intramuscular injections of LSD. The intramuscular route is useful for studying the effects of LSD on chronic schizophrenics, and reactions are noted in approximately 30 minutes.

2. Tolerance to LSD in chronic schizophrenics is evidenced on the second and complete on the third day of drug administration. A period of 4 to 6 days free of LSD is necessary to reinstate the original reaction to LSD.

3. The gross behavioral reactions of chronic schizophrenics affords a useful index of tolerance. Estimates of the LSD effect can be made with the use of the rating scale which has been described.

4. The behavioral difference between intramuscular LSD and intramuscular mescaline is not pronounced in chronic regressed schizophrenic patients. That tolerance is not purely psychologic is indicated by the fact that there is no cross-tolerance between mescaline and LSD, whereas cross-tolerance is shown between LSD and LAE, and brom-lysergic acid.

5. Clinical responses of chronic schizophrenics to LSD can be categorized as: (a) *covert:* In which the patient may show a delayed reaction; (b) *intensification:* where the patient reacts by a regression to earlier forms of behavior, or a magnification of symptoms; (c) *reversal:* in which the manifestations of the drug reaction are quite the reverse of the usual behavior.

6. While the reaction to LSD is shown by the use of control studies to be due to the LSD rather than the experimental procedure itself, nevertheless there are indications that the reaction may be determined in part by the milieu.

BIBLIOGRAPHY

1. Belsanti, R.: Modificazioni neuro-psico-biochimiche indotte dalla dietilamide dell-'acido lisergico in schizofrenici e frenastenici. *Acta Neurol.* (*Ital.*), *7:* 340, 1952.
2. Bleuler, M.: Address to the Washington Psychiatric Society, 1950.
3. Busch, A. K., and Johnson, W. C.: LSD 25 as an aid in psychotherapy. *Dis. Nerv. System, 11:* 241, 1950.
4. Condrau, G.: Klinische Erfahrungen an Geisteskranken mit Lysergsaure-Diathylamid (Clinical experiences in mental patients with lysergic acid-diethylamide). *Acta Psychiat. et Neurol. Scand., 24:* 9, 1949.
5. DeGiacomo, U.: Catatonie toxique experimentale. *Acta Neurol. Milano 6,* No. 1, 1951.
6. Forrer, G. R., and Goldner, R. D.: Experimental physiological studies with lysergic acid diethylamide (LSD25). *Arch. Neurol. & Psychiat., 65:* 581, 1951.
7. Hoch, P. H., Cattell, J. P., and Pennes, H. H.: Effects of mescaline and lysergic acid (d-LSD-25) *Am. J. Psychiat., 108:* 579, 1952.
8. Hoch, P. H.: Comments, Experimental psychiatry. *Am. J. Psychiat., 111:* 787, 1955.
9. Hoffer, A., Osmond, H., Smythies, J.: Schizophrenia: A New Approach. *J. Ment. Sci., 100:* 29 ~~418~~, 1954.
10. Liddell, D. W., and Weil-Malherbe, H.: The effects of methedrine and of lysergic acid diethylamide on mental processes and on the blood adrenaline level. *J. Neurol., Neurosurg. & Psychiat., 16:* 7, 1953.
11. Mayer-Gross, W.: Experimental psychoses and other mental abnormalities produced by drugs. *Brit. M. J., 2:* 317, 1951.
12. Pennes, H. H.: Clinical reactions of schizophrenics to sodium amytal, pervitin hydrochloride, mescaline sulfate, and *d*-lysergic acid diethylamide (LSD-25). *J. Nerv. Ment. Dis. 119:* 95, 1954.
13. Rinkel, M., DeShon, H. J., Hyde, R. W., and Solomon, H. C.: Experimental schizophrenia-like symptoms. *Am. J. Psychiat., 108:* 572, 1952.
14. Sloane, B., Doust, J. W. L.: Psychophysiological investigations in experimental psychoses: results of the exhibition of D-lysergic acid diethylamide to psychiatric patients. *J. Ment. Sci. 100:* 129, 1954.
15. Stoll W. A.: Lysergsaure-diathylamid, ein Phantastikum aus der Mutterkorngruppe (Diethylamide of lysergic acid; an unusual derivative of ergot). *Schweiz. Arch. f. Neurol. u. Psychiat., 60:* 279, 1947.

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BLOOD PRESSURE, PLASMA PEPSINOGEN, AND BEHAVIOR IN CATS SUBJECTED TO EXPERIMENTAL PRODUCTION OF ANXIETY[1]

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WITH THE TECHNICAL ASSISTANCE OF JAMES BEAUMONT AND VIRGINIA HAGGAR

INTRODUCTION

Despite considerable evidence that psychological stimuli produce acute vasoconstriction and elevation in blood pressure, and that these mechanisms account for certain of the variations in the clinical course of hypertensive vascular disease in man, the hypothesis that anxiety and behavioral disturbances are of significant importance in the etiology of chronic hypertension has not been substantiated by empirical studies (2). Clinical data defining the personality types of patients with the disease or illustrating temporal relationships between significant emotional experiences and the onset of hypertension or its exacerbations are usually derived retrospectively, nor do they easily lend themselves to statistically valid conclusions concerning psychogenesis. Direct experimental demonstration that continuous or repeated psychological trauma can produce chronic vasoconstriction and permanent injury is obviously impossible in the human and difficult to analogize in animal studies. In the latter respect, several investigators have reported development of elevation of blood pressure in rats, with the use of continuous audiogenic stimulation (3, 15), but this trauma is hardly equivalent to that assumed to be of significance in man while the elevation is slight and not always sustained.

Although the precise relationships of experimental neuroses in animals to the behavioral disturbances of man need considerable clarification, these conditions do possess certain features in common, among the most important of which is chronic anxiety. It seemed reasonable therefore that the experimental neuroses might be exploited to investigate psychosomatic mechanisms in a controlled manner in animals, and accordingly a series of researches has been devised to study the *chronic* effects of conditioning techniques on the vascular system of a number of animal species.

The present report constitutes an evaluation of blood pressure changes in cats in whom the technique described by Masserman for production of experimental neuroses in these animals was employed (9). Normal cats as well as those subjected to minor degrees of renal injury, insufficient in themselves to produce hypertensive disease, were studied. The latter condition was imposed in the belief that since severe impairment of renal function leads to hypertensive disease, either by resulting in the elaboration of vasoconstrictor agents or the failure of inhibition of extrarenal vasoconstrictive influences (5, 4), a minor renal injury might potentiate the effect of psychologic stress on the vascular system. Thus if emotionally traumatic experiences are not capable of directly producing chronic hypertensive disease in the previously normal subject, they may at least play a role in potentiation and exacerbation of the disease, a phenomenon which has been frequently suggested in clinical studies (13).

In addition to studies of blood pressure in these animals, the level of plasma pepsinogen was determined repeatedly. The titer of this substance represents a measure of gastric activity and is increased in individuals with peptic ulcer and perhaps in response to stress (10). If pepsinogen levels are indeed correlated with anxiety in a non-specific fashion, they should rise in conjunction with other physiologic manifestations of the stress reaction such as elevation of blood pressure. On the other hand, if as Alexander (1) has proposed and Mahl (8) has disputed, the hypothesis of Cannon concerning the effects of acute emotional trauma can be carried over to chronic anxiety states, the pepsinogen levels and blood

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[1] Supported by grants from the Public Health Service, M-739 and H-1954.

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pressure levels might be expected to vary inversely.

MATERIALS AND METHODS

Thirty-six cats were studied of whom seven were subjected to the experimental procedures designed to produce neuroses. Most of the animals were full-grown strays received from the local animal shelter. A few had previously been house pets or were received when kittens and raised in the laboratory. With one exception, all were females. They were housed indoors, two to three to a cage, and were fed with commercial cat food. The cages were 6 x 4 x 4 feet, provided with shelf-platforms, and allowed ample room for activity.

Blood pressures were determined with the animal restrained on its back on a board. The femoral artery was punctured directly with a 21 gauge needle and the mean blood pressure read on a mercury manometer. Comparison of the results achieved with this technique and with cannulation of the femoral and carotid artery with an 18 gauge cannula revealed identical results. Determinations were made as often as every two to three weeks, and at this frequency permanent damage to the artery did not occur.

A conditioning cage similar to that described by Masserman was employed for the behavioral studies (9). Cats were trained to feed themselves by lifting the lid of a container at one end of the box in response to a light or buzzer stimulus. When this pattern was firmly established, the animal was exposed at irregular intervals to an air blast of about 10 lb. pressure, or an electric shock, both of which were activated by the lifting of the lid. Prior to the administration of the traumatic stimulus most of the cats were taught to operate a switch at the opposite end of the cage which controlled the light or buzzer stimulus, and thus were able to activate the feeding cycle entirely by themselves. Three of the animals were trained to discriminate between a positive stimulus for food (light) and a negative stimulus (buzz), and were later traumatized when responding to the former.

Two cats in the group of 36 were unilaterally nephrectomized, and one of these was conditioned (#13). In three animals, a figure-of-eight ligature was placed around one kidney; two of these (#5 and #14) were conditioned. In two control animals, a figure-of-eight ligature was placed around one kidney, and the contralateral organ was removed, while two animals were placed on a low choline diet for a two-week period following weaning. These latter procedures were performed in order to study the effects on the blood pressure of the cat of methods for production of experimental hypertensive vascular disease which have been successful in other species (6).

The method of Mirsky and associates was employed for determination of plasma pepsinogen (11), and it was demonstrated that at least 90 per cent of added pepsin could be recovered from the cat plasma. The error of the method in our hands amounted to approximately 10 per cent. Plasma specimens were drawn each time the blood pressure was determined, and in addition several acute studies were done immediately before and after the conditioned animals were placed in the experimental cage. It was established that neither fasting nor food intake had any significant effect on pepsinogen levels; however, except for the acute experiments, all plasma specimens were drawn with the cat in the fasting state.

RESULTS

A. Control blood pressures

The results in 34 of the cats are set forth in table 1. The average blood pressure of all cats at the initial determination, usually made within a few days after arrival at the laboratory, was 155 mm. Hg with a standard deviation of ±23 mm. Hg. Except for a few instances, the average blood pressure for each cat showed little change from this initial determination. Their over-all average was 164 ± 19 mm. Hg, a figure not significantly different from the average of initial determinations. Moreover, the blood pressure for each cat was fairly consistent during the period of study, the average standard deviation being 11 mm. Hg.

Light anesthesia with 30 to 90 mg. of nembutal administered intravenously produced inconsistent effects on blood pressure, some cats showing an increase and others a slight decrease.

The results in the four control animals from

TABLE 1.—INITIAL AND AVERAGE BLOOD PRESSURE OF ALL CATS

Cat No.	Initial Blood Pressure	Average Blood Pressure				B.P. with Anesthesia
		B.P.	S.D.†	No. of determinations	Duration of observation	
	mm. Hg	*mm. Hg*			*months*	*mm. Hg*
2	170	150	±19	16	5	135
3	160	189	10	27	19	175;183
5	145	120	9	7	2	—
6	145	141	15	6	2	—
8	110	113	22	6	2	—
9	90	—	—	1	7	—
12	140	149	8	15	7	158
13	150	153	15	7	2	—
14	155	164	11	10	4	—
15*	170	169	4	7	7	190;183;158
16	135	148	8	2	2	—
17	180	169	10	6	2	180
18	190	183	8	4	2	158
19	130	—	—	1	—	—
20	145	148	12	5	3	—
21	158	174	10	15	13	185
22	185	170	12	16	8	155
23	155	—	—	1	—	—
24	190	192	5	6	3	178
25	145	—	—	1	—	—
26	165	—	—	1	—	—
27	160	180	11	5	4	185
28	170	186	18	15	11	180
29	145	154	13	2	1	165
30	165	174	13	10	11	190
31	138	148	14	2	2	—
32	135	167	13	11	10	175
33	160	174	7	4	3	160;160
34	178	177	3	2	1	—
35	120	—	—	1	—	—
36	158	161	4	2	3	165;168
39	170	175	3	2	1	—
40	165	—	—	1	—	135
41	198	179	11	5	2	—
Average........	155.1 ± 23.1	163.9 ± 19.0	11.2			

* Male.

† Standard deviation = $\sqrt{\dfrac{\Sigma(x^2) - \dfrac{\Sigma x^2}{n}}{n - 1}}$.

TABLE 2.—CHANGES IN BLOOD PRESSURE IN CATS SUBJECTED TO OPERATIVE AND DIETARY PROCEDURES

Cat No.	Average Blood Pressure	SD/n*	B.P. with Anesthesia	Procedure Performed	Average B.P. after Procedure	SD/n	B.P. with Anesthesia
	mm. Hg		*mm. Hg*		*mm. Hg*	*mm. Hg*	
2	150	±19/16	135	Right nephrectomy	157	±12/6	—
12	149	8/15	158	Right fig.-of-8	158	8/25	170
33	174	7/14	160	Rt. fig.-of-8; left nephrectomy	199	11/6	187
40	165	—	135	Rt. fig.-of-8; left nephrectomy	193	3/2	195
37				Both animals fed low choline diet for 2 weeks after weaning	159	10/5	—
38					165	6/5	—

* n = number of determinations.

the group of 34 who were subjected to renal surgery are indicated in table 2. Data on the two additional animals who were fed a low choline diet are included in this table. Unilateral nephrectomy in one cat produced no significant changes; unilateral figure-of-eight tie resulted in a slightly increased pressure in another, but this pressure was still within the over-all average of all the animals. The low choline diet had no appreciable effect.

Unilateral figure-of-eight tie followed by removal of the contralateral kidney, in two animals, produced pressures consistently over 190 mm. Hg in both, and these pressures were unaffected by anesthesia. Both animals remained well and did not develop azotemia.

B. Behavioral changes

Seven cats in the group listed in table 1 were subjected to conditioning procedures. These were #'s 5, 6, 8, 13, 14, 15, 16. A detailed report of their behavior will be presented elsewhere; for the purposes of this discussion the results have been summarized. Although the results varied somewhat among the individual animals, certain generalizations can be made:

1) The cats easily learned to manipulate the lid of the food box, accomplishing this maneuver within a few days after onset of conditioning. They rapidly lost any initial fear or avoidance of the experimental cage and were eager to enter it. This was most marked, to the point of intense hyperactivity, in cat #16, who previously had been a house pet of the experimenter.

2) Self-activation of the light and/or buzzer switch was learned easily by five of the six cats to whom it was taught. The sixth animal (#13) showed resistance but was, on the other hand, taught to make a circle around the cage, in the same direction each time, before responding to the conditioned stimulus.

3) Following presentation of the air blast, all animals initially retreated from the food box, usually to crouch in the rear of the cage. By repeated presentation of the conditioned stimulus, the cats could be coaxed to again approach the food box. After several pairings of blast with the conditioned stimulus the learned response was usually completely eliminated. Cat #13, however, periodically fed despite the blast by pawing the food from the box, while cat #15 eventually ignored the blast entirely while feeding. In both these animals, addition of electric shock resulted in complete inhibition.

4) The severity of the fear reaction to the initial pairings of the conditioned stimulus and air blast and/or shock varied from moderate to slight. The most striking manifestation was excessive washing activity which occurred in all animals. Acute fear, manifested by crouching in the rear of the cage, dilatation of the pupils, and vocalization were evident, and occasionally the animal would seek escape from the cage. Cat #8 displayed the most pronounced reactions in this respect.

5) Avoidance of the food box following repeated air blast, or when necessary blast plus electric shock, was present in all the animals. When repeated trauma resulted in complete inhibition of the conditioned response, with the cats remaining inactive in the rear of the cage, prolongation of hunger counteracted this to only a limited extent even when continued for as long as ten days in two animals (#13 and #14).

6) Manual presentation of the conditioned stimulus after the air blast and/or shock exposure did not elicit the type of startle reactions and exacerbation of anxiety symptoms described by Masserman.

7) Behavior of the animals outside of the experimental cage, both in relationship to fellow cats and to the experimenter, was not noted to change significantly during the course of the experiments. Several of the animals seemed briefly to "court affection" from the experimenter in the manner described by Masserman.

8) Retraining following complete elimination of the response to the conditioned stimulus was accomplished easily with little greater effort than was employed initially. In several of the animals, this was done repeatedly; the response was established, eliminated, reestablished, etc. without any evidence of further behavioral change. Nor was the ease of retraining significantly affected by whether the intervals of rest following the traumatic experience were several days or months.

9) One cat (#5), who was taught to discriminate between positive and negative stimuli to obtain food, was given her only daily

ration in the experimental cage for a period of six months and showed no evidence of breakdown or loss of efficiency in the task. This animal then received air-blasting following the presentation of the positive conditioned stimulus, inhibited the response, and was retrained to discriminate. This cycle was repeated five times over the course of a year with no significant changes in over-all behavior.

C. Blood pressure changes during conditioning periods

The changes in blood pressure in the seven cats who were conditioned are presented in table 3. Cats #6, #8, and #16 displayed a significant rise in their blood pressure although the levels reached were well within the range of the control group. All three animals died, #8 following surgery, and #6 and #16 probably of feline enteritis, an acute virus ailment of cats, which was prevalent in the colony at the time. No significant vascular lesions were detected in sections of the heart or kidneys. It is of interest to note that cat #8 which showed a considerable elevation had previously been a well-cared for house pet, and was the animal who showed the most marked fear during the presentation of the traumatic stimulus. On the

TABLE 3.—EFFECTS OF CONDITIONING ON BLOOD PRESSURE AND PEPSINOGEN

Cat No.	Period	Duration of Period	Average Mean Blood Pressure	Standard Error*	"p" Value of Difference†	Plasma Pepsinogen (µg Tyrosine Released/cc. Plasma)	Standard Error*	"p" Value of Difference†	Remarks
		months	*mm. Hg*						
6	Control	2	141	8.8	.05> .02	—			Died of infection
	Conditioning	4	162	2.0		632 762 (a)	12	<.01	a) blast period
						503 (b)	32		b) inhibitory period
8	Control	1½	113	12.9	.01> .001	—			
	Conditioning	6	155	2.8		447	64		Died post-op.
16	Control	2	148	4.7	.01> .001	499	85		Died of infection
	Conditioning	3	188	7.9		364	39		
5	Control	2	120	4.5	.02	—			
	Conditioning	10	132	2.2		602	46		
	After Rt. 8	3	146	4.7	.015	605	182		
	Cond. after Rt. 8	2	149	14.0		420	59		
	Rest	4	133	1.7		658	108		
	Conditioning	3	128	3.0		566	9		
13	Control	2	153	7.5		485	85	.05	
	Conditioning	5	166	2.3		279	36		
	Conditioning after Rt.Np.	9	172	2.4		394	49		
	Rest	6	160	3.0		496	38		
14	Control	4	164	3.6	.015	559	56		
	Conditioning	4	164	3.0		662	92		
	Cond. after Rt. 8	9	174	2.3		623	86		
	Rest	6	169	4.7		460	54		
15	Control	7	169	1.8	.05	525	75		
	Conditioning	10	175	2.3		514	55	.05	
	Rest	6	180	4.1		337	51		

* Standard error $= \sqrt{\dfrac{\Sigma(x^2) - \dfrac{\Sigma x^2}{n}}{n(n-1)}}$.

† "p" value listed only when differences are significant.

other hand, cat #16, also a previous house pet, displayed a rise despite the fact that her death occurred *before* the traumatic situation (i.e., air blast) was introduced.

In the remaining four animals, changes were of minor biologic importance even in those instances where statistical significance was apparent. A slight rise occurred in #5 when first conditioned; blood pressure rose still further after a figure-of-eight ligature was placed on the right kidney, but subsequent conditioning produced no further change, while pressures during all periods remained at the lower limits of the range for the entire group. Significant changes in #13 were absent. The slight rise which occurred in #14 following conditioning after a figure-of-eight tie was probably due to the latter procedure. In #15 the change was more pronounced; blood pressure rose during conditioning, and the rise persisted during the rest period.

D. Plasma pepsinogen

1. *Conditioning studies.* The average levels of plasma pepsinogen in the conditioned animals during each period are presented in table 3. Significant increases during conditioning did not occur; rather there was a tendency for the level to decrease, a change which was significant in several animals. In cat #6, the conditioning period could be broken down to an interval during which the animal was responding and receiving the traumatic stimulus (blast period) and an interval during which she was inhibiting to the stimulus (inhibitory period). During the latter interval, pepsinogen decreased significantly.

The changes in pepsinogen levels during several acute experiments are set forth in table 4. Two types of experiments were performed:

1) Pepsinogen was determined in two cats (#13 and #14) who had developed complete inhibition to the conditioned stimulus and refused to eat during a four-day period in the experimental cage. In both, the level of pepsinogen declined.

2) In four animals, pepsinogen was determined immediately before and after the daily conditioning period, both during times when conditioning alone was being employed and when a traumatic stimulus was in use. This was done repeatedly in cat #5. On almost all occasions, any changes which occurred were in the downward direction and were not of significantly greater severity when the traumatic stimulus was employed.

TABLE 4.—ACUTE CHANGES IN PEPSINOGEN LEVELS

I. Four day studies

Length of Exposure to Cage	Pepsinogen	
	Cat #13	Cat #14
Before	462	860
24 hours	450	—
48 hours	—	—
72 hours	322	—
96 hours	—	440
24 hours after release	380	880

II. Immediate pre- and post-conditioning studies

Cat No.	Pepsinogen		Pepsinogen	
	Before exposure	After exposure	Before exposure	After exposure
	(Conditioning alone)		(Conditioning and traumatic stimulus)	
5	875 478 585 596	575 383 538 560	585 463 598	475 413 578
13	384	332	284	341
14	350	358	862 684	522 359
15	463	298	604	536

III. Control feeding and fasting studies

Effect of fasting

Cat No.	Length of Fast	Pepsinogen
3	24 hours	250
	48 hours	295
	72 hours	245
	96 hours	340

Effect of feeding

Cat No.	Time after Feeding	Pepsinogen
28	24 hr. fast	279
	30 min. after food	283
32	24 hr. fast	445
	2 hr. after food	500
	8 hr. after food	410

The effects on plasma pepsinogen of feeding and fasting in control animals are also presented in table 4. Significant changes did not occur.

2. *Comparison of level of plasma pepsinogen and blood pressure.* The average level of pepsinogen during the entire study for each cat, including control animals in whom it was determined, was graphed against its average blood pressure (figure 1), and it was noted that those cats with higher blood pressure levels tended to have lower pepsinogen values and *vice versa*. Using the average blood pressure of 164 mm. Hg and the average pepsinogen value of "normals" of 400 μg. tyrosine/cc. (11) as the points of separation of these continuous variables, a chi square analysis was performed, which indicated that this separation into a "high pepsinogen-low blood pressure" group, and a "low pepsinogen-high blood pressure" group was significant with a p value of .017. When the blood pressure and level of pepsinogen for each determination in 15 of the cats during a control period of six months were treated similarly (figure 2), the separation was more strikingly significant with a p value of less than .001. An inverse relationship between pepsinogen level and blood pressure as a characteristic of the animals therefore definitely seemed indicated by the data.

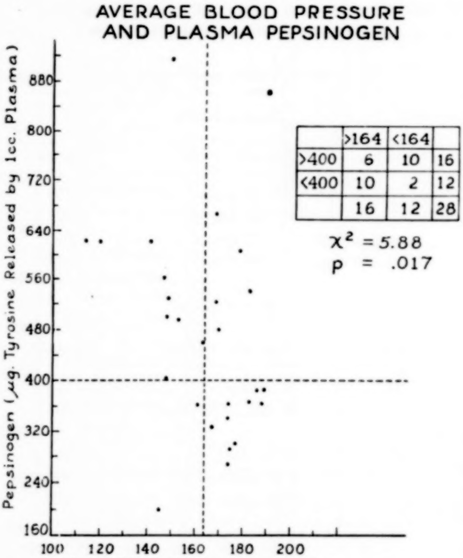

FIG. 1. Chart illustrates the grouping of cats into a "low pepsinogen, high blood pressure" group and a "high pepsinogen, low blood pressure" group. Each point represents an average of all blood pressure and pepsinogen determinations on a single cat.

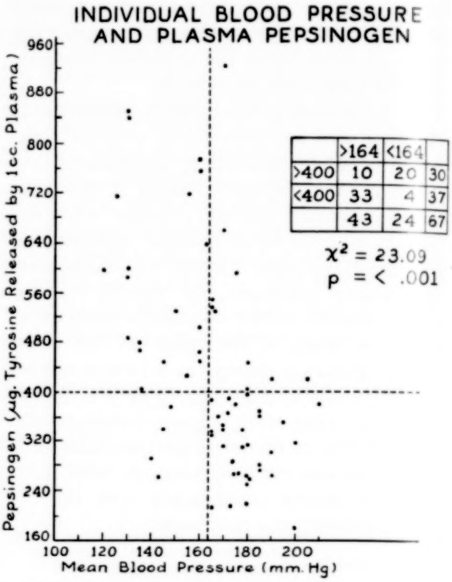

FIG. 2. Chart illustrates the same grouping as described in figure 1. Each point represents a single simultaneous blood pressure and pepsinogen determination.

3. *Pathologic examination.* Gross and microscopic examinations of stomach and duodenum in cats #6, 18, 16, and 15 and in those of the normal animals who were sacrificed revealed no evidence of ulceration.

DISCUSSION

These studies were intended primarily as an exploration of the applicability of methods of producing chronically disturbed behavior in animals to the investigation of psychosomatic mechanisms, particularly those concerned with hypertensive vascular disease. As such they offer several leads which may be promising, while in other respects are somewhat disappointing. Of particular interest are the results noted in three areas: 1) the meaning of "experimental neurosis" as achieved in cats with the Masserman techniques; 2) the blood pressure of the unanesthetized cats under "normal" circumstances and under the stress of chronic anxiety; 3) the apparent difference between the behavior of blood pressure and pepsinogen levels under the impact of anxiety and the possible relationship of this fact to certain psychosomatic mechanisms.

1) Changes in behavior. It was not the purpose of this study to attempt to confirm or deny the concept of experimental neuroses in cats. However, although we observed most of the acute phenomena which Masserman has described, it seemed clear to us that a chronic change in behavior was not produced. As Watson (16) has so well pointed out in studies designed to repeat Masserman's work, neurosis in terms of chronic maladaptive behavior was not evident in the animals. Rather the reaction of the cats was adaptive to the situation whether they learned to overcome the traumatic situation or to avoid it completely by retreat. In either case it could be considered a "healthy" reaction and, apparently, one confined only to the acute experiment in the cage, with no change in over-all behavior. It is undoubtedly true that minor variations were present between the technique we employed and that originally described by Masserman. It seems likely, however, that the differences in results are explained more rationally as due to differences in interpretation of data. A more detailed report of these features of the present study will be presented elsewhere. It is sufficient here to say that it was our impression that the hunger-fear conflict was mainly of value to produce acute fear or anxiety repeatedly in the animal, with little if any chronic disturbance, and as such may have been of no greater significance to the animal than the repeated exposure to the trauma of blood pressure determination.

2) Changes in blood pressure. Root has published the results of single blood pressure determinations under dial-urethane anesthesia in a large series of cats, but similar data in the unanesthetized cat have not been reported previously (14). The average level seems quite high as compared with other species which have been studied although considerable variation among different cats exists.

In contrast to dogs, the cats continued to offer resistance to restraint on the animal board and could not be trained to accept the procedure despite repeated determinations and despite attempts to soothe them. Once tied down, however, with the needle in the artery, they did not struggle.

The question nevertheless arises as to whether these values represent the usual blood pressure of the unanesthetized cat, or whether the procedure of determination itself introduces the elevation. The fact that light anesthesia had little if any effect militates against the latter possibility and suggests that the elevation was at least not an immediately transient one. Captivity or the living circumstances *per se* did not appear to exert an appreciable effect since variations within each animal, sometimes over periods of as long as 18 months, were slight.

Kaindle and Von Euler have pointed out that nor-adrenaline constitutes 75 per cent of the secretion of the cat's adrenal even at rest and have demonstrated elevations in mean blood pressure from initial levels of 160 mm. Hg to well over 200 mm. Hg, along with further increase of nor-adrenaline secretion, in response to carotid sinus stimulation (7). It has also been demonstrated by Page that the blood pressure response of normal cats to serotonin is markedly depressor, differing in this respect from that usually observed in dogs and man, while resembling that seen in neurogenic hypertensive dogs. The cat also has a marked depressor response following administration of tetraethylammonium chloride (12). Page's data thus suggest that a considerable neurogenic component operates to maintain blood pressure in the cat. Either of these mechanisms might account for the relatively high levels which we observed. On the other hand, if this elevation is indeed artificial and does not represent the blood pressure which the cat displays in its usual environment, it is worthy of note that it occurs with such comparative ease.

These elevated levels of blood pressure do not appear to be associated with or to produce changes of hypertensive vascular disease. Pathological specimens of heart and kidney from eight of the control animals who died of unrelated causes, or were sacrificed, have revealed no vascular lesions.

The accuracy of mean blood pressure determined with a mercury manometer can be questioned. That it is not responsible, however, for the high readings was demonstrated by checking the blood pressure in two animals with a strain gauge manometer. The pressure obtained ranged from 154/108 to 200/135 mm. Hg in one (#14) and 160/116 to 188/128 mm. Hg in the other (#13).

Unilateral renal injury and choline-deficient diet did not have significant effects. The figure-of-eight tie of the kidney with contralateral nephrectomy, however, did produce findings similar to those observed in the dog and rat following this procedure (6) and represents what is probably the actual picture of hypertensive vascular disease in the cat.

The data from the control animals thus make it unlikely that the changes in blood pressure which occurred in the disturbed cats indicated the development of actual hypertensive vascular disease during the period of the study. Inasmuch as the blood pressure in individual control animals was relatively constant, the elevations which developed in cats #6, #8, and #16 were probably meaningful but, as in similar investigations in man, leave unanswered the primary question of whether repeated acute vasoconstriction of this type can lead to the vasoconstrictive pathology of chronic hypertension. Nor was it possible to derive any data to indicate whether minor renal injury might produce an increased sensitivity to chronic stress. The results do indicate that techniques of animal research can be applied to further chronic studies of this problem. It would seem, however, that cats, in view of their high level of blood pressure and the difficulties in their management, constitute a relatively poor species for such studies.

3) Changes in levels of plasma pepsinogen and their relation to blood pressure. Contrary to the results which have been reported in patients with peptic ulcer, significant increases in plasma pepsinogen with stress, either acute or chronic, did not occur. Changes which were noted were of meager significance and demonstrated a downward trend, particularly with acute disturbances. Quite striking, however, was the separation of the cats into two groups, differentiated by a pattern of high pepsinogen and less than average blood pressure in one group and the inverse relationship in the other.

It is generally assumed that the type of emotional disturbance determines organ specificity in chronic psychosomatic disorders. According to this thesis, since aggressive behavior, anger, and fear elicit acute reactions in the sympathetic nervous system, whereas passivity and oral dependent behavior bring forth disturbances in organs innervated by the parasympathetic system, prolongation of these specific emotional disturbances produces chronic damage to the respective organs which are involved (1). Some investigators have argued, however, that this relationship cannot be carried over to chronic states of anxiety (8).

The studies herein presented did not demonstrate significant permanent changes either in the cardiovascular system or in the stomach and duodenum. However, the conditioning techniques which were employed did not produce chronic behavioral disturbances, accomplishing merely repeated exposure to acute anxiety. The need for further methodological advances in this area therefore is indicated. Minimal acute changes were noted, with pepsinogen declining and blood pressure rising, and these effects, although unassociated with chronic injury, occurred in situations where acute fear, anger, and aggressive behavior were the predominant emotional patterns. These observations, however, offer no additional insight into the problem of whether acute changes will lead to chronic disorders.

Most interesting, however, was the demonstration of a clear-cut separation of the group of cats as a whole into "sympathetic types" and "parasympathetic types" based upon measurable biochemical and physiologic characteristics—namely the inverse relationships between blood pressure and pepsinogen—which were not appreciably affected by the impact of stress. These latter data indicate that prior organ susceptibility must be considered in determining organ specificity in psychosomatic diseases. To be sure, such organ susceptibility may have been established ultimately by early developmental experiences, and not only by constitutional or genetic determinants. Once established, however, chronic behavioral disturbance, even when appropriately designed to reproduce specific psychodynamic patterns and continued for a sufficiently long period of time, may be ineffective if applied to the inappropriate type; *viz.*, a chronic stimulus evoking fear and anger may produce no change when the exposed animal is the "parasympathetic type", whereas the same stimulus applied to the "sympathetic type" might cause vascular disease.

SUMMARY AND CONCLUSIONS

Studies were performed to determine the possibility of investigating psychosomatic mechanisms related to hypertensive vascular disease by producing experimental behavioral disturbances in animals. The test animal was the cat, and the techniques of Masserman for inducing experimental neurosis were employed to stress these subjects. In addition to blood pressure, plasma pepsinogen was determined in order to measure the simultaneous manifestations of the stress reaction on a second organ system. The following findings were elicited:

1) The conditioning techniques did not produce neurotic behavior but resulted rather in development of acute anxiety limited to the experimental cage and of adaptive responses to the traumatic stimuli.

2) Blood pressure in normal cats was noted to be high as compared to other animal species, but could be elevated further by renal damage.

3) Blood pressure increased slightly in several of the animals who were conditioned, but the rise was not above levels seen spontaneously in control animals and was not associated with permanent vascular damage.

4) Plasma pepsinogen did not rise with either acute or chronic stress, but rather tended to decline.

5) A clear-cut separation of the animals into a group with high pepsinogen levels and less than average blood pressure, and into a group with low pepsinogen and higher than average blood pressure was noted.

The studies indicated that techniques of animal conditioning are applicable to the investigation of psychosomatic mechanisms. The cat, however, as a subject for studying blood pressure change was considered unsatisfactory. The inverse relationship between blood pressure and plasma pepsinogen in the group as a whole indicated a division of the subjects into "sympathetic types" and "parasympathetic types" and offered insight into the understanding of organ specificity in psychosomatic disorders.

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BIBLIOGRAPHY

1. Alexander, F.: *Psychosomatic Medicine*. New York: W. W. Norton & Co., 1950.
2. Binger, C.: On so-called psychogenic influences in hypertension. *Psychosom. Med., 13:* 273, 1951.
3. Farris, E. J., Yeakel, E. H., and Medoff, H. S.: Development of hypertension in emotional gray Norway rats after air-blasting. *Am. J. Physiol., 114:* 331, 1945.
4. Floyer, M. A.: The role of the kidney in the mechanism of experimental hypertension. In *Ciba Foundation Symposium on Hypertension,* edited by Wolstenholme, G. E. W., and Cameron, M. P., p. 155. Boston: Little, Brown, and Co., 1954.
5. Grollman, A.: Experimental studies on hypertension. In *Hypertension; A Symposium,* p. 22. Minneapolis: University of Minnesota Press, 1951.
6. Grollman, A.: A simplified procedure for inducing chronic renal hypertension in the mammal. *Proc. Soc. Exper. Biol. & Med., 57:* 102, 1944.
7. Kaindle, F., and Von Euler, U. S.: Liberation of nor-adrenaline from the suprarenal glands of the cat during carotid occlusion. *Am. J. Physiol., 166:* 285, 1951.
8. Mahl, G. F.: Physiologic changes during chronic fear. Symposium: Comparative conditioned neuroses. *Ann. N. Y. Acad. Sc., 56:* 240, 1953.
9. Masserman, J. H.: *Behavior and Neuroses*. Chicago: Univ. of Chicago Press, 1943.
10. Mirsky, I. A., Kaplan, S., and Broh-Kahn, R. H.: Pepsinogen excretion (uropepsin) as an index of the influence of various life situations on gastric secretion. *Proc. A. Research Nerv. & Ment. Dis., 29:* 628, 1950.
11. Mirsky, I. A., Futterman, P., Kaplan, S., and Broh-Kahn, R. H.: Blood plasma pepsinogen. I. The source, properties, and assay of the proteolytic action of plasma at acid reactions. *J. Lab. & Clin. Med., 40:* 17, 1952.
12. Page, I. H.: Neural and humoral control of blood vessels. In *Ciba Foundation Symposium on Hypertension,* edited by Wolstenholme, G. E. W., and Cameron, M. P., p. 3. Boston: Little, Brown, and Co., 1954.
13. Reiser, M. F., Rosenbaum, M., and Ferris, E. B.: Psychologic mechanisms in malignant hypertension. *Psychosom. Med., 13:* 147, 1951.
14. Root, M. A.: Mean blood pressure of cats under dial-urethane anesthesia. *Am. J. Physiol., 162:* 308, 1950.
15. Rothlin, E., Emmenagger, H., and Cerletti, A.: Versuche zur erzeugung audiogenier hypertonie an ratten. *Helva. Physiol. Acta, 11:* 25, 1953.
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BIBLIOGRAPHY

1. Alexander, F.: *Psychosomatic Medicine*. New York: W. W. Norton & Co., 1950.
2. Binger, C.: On so-called psychogenic influences in hypertension. *Psychosom. Med., 13:* 273, 1951.
3. Farris, E. J., Yeakel, E. H., and Medoff, H. S.: Development of hypertension in emotional gray Norway rats after air-blasting. *Am. J. Physiol., 114:* 331, 1945.
4. Floyer, M. A.: The role of the kidney in the mechanism of experimental hypertension. In *Ciba Foundation Symposium on Hypertension*, edited by Wolstenholme, G. E. W., and Cameron, M. P., p. 155. Boston: Little, Brown, and Co., 1954.
5. Grollman, A.: Experimental studies on hypertension. In *Hypertension; A Symposium*, p. 22. Minneapolis: University of Minnesota Press, 1951.
6. Grollman, A.: A simplified procedure for inducing chronic renal hypertension in the mammal. *Proc. Soc. Exper. Biol. & Med., 57:* 102, 1944.
7. Kaindle, F., and Von Euler, U. S.: Liberation of nor-adrenaline from the suprarenal glands of the cat during carotid occlusion. *Am. J. Physiol., 166:* 285, 1951.
8. Mahl, G. F.: Physiologic changes during chronic fear. Symposium: Comparative conditioned neuroses. *Ann. N. Y. Acad. Sc., 56:* 240, 1953.
9. Masserman, J. H.: *Behavior and Neuroses*. Chicago: Univ. of Chicago Press, 1943.
10. Mirsky, I. A., Kaplan, S., and Broh-Kahn, R. H.: Pepsinogen excretion (uropepsin) as an index of the influence of various life situations on gastric secretion. *Proc. A. Research Nerv. & Ment. Dis., 29:* 628, 1950.
11. Mirsky, I. A., Futterman, P., Kaplan, S., and Broh-Kahn, R. H.: Blood plasma pepsinogen. I. The source, properties, and assay of the proteolytic action of plasma at acid reactions. *J. Lab. & Clin. Med., 40:* 17, 1952.
12. Page, I. H.: Neural and humoral control of blood vessels. In *Ciba Foundation Symposium on Hypertension*, edited by Wolstenholme, G. E. W., and Cameron, M. P., p. 3. Boston: Little, Brown, and Co., 1954.
13. Reiser, M. F., Rosenbaum, M., and Ferris, E. B.: Psychologic mechanisms in malignant hypertension. *Psychosom. Med., 13:* 147, 1951.
14. Root, M. A.: Mean blood pressure of cats under dial-urethane anesthesia. *Am. J. Physiol., 162:* 308, 1950.
15. Rothlin, E., Emmenagger, H., and Cerletti, A.: Versuche zur erzeugung audiogenier hypertonie an ratten. *Helva. Physiol. Acta, 11:* 25, 1953.
16. Watson, R. E.: Experimentally induced conflict in cats. *Psychosom. Med., 16:* 340, 1954.

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ELECTROENCEPHALOGRAPHY AND NEURORADIOLOGY IN THE DIAGNOSIS OF ORGANIC MENTAL CONDITIONS[1]

ALDO MORELLO, M.D., AND SIDNEY MERLIS, M.D.

Etiological factors in certain mental disorders continue to remain vague and obscure. Such factors run the gamut from physiological to psychological. Those physicians involved in the various neuropsychiatric disciplines often approach the diagnosis of similar mental disorders from opposite standpoints. The diagnostic opinions thereby are often as numerous as the physicians involved.

Because of the very nature of neuropsychiatric conditions the diagnosis has in the past almost always relied on subjective signs and symptoms. Such subjective evaluation often is inadequate because of the lack of a definite baseline for comparison. Recent advancements and improvements in technique have led to the development of objective tests which permit a more accurate appraisal of certain diagnostic problems. As we learn more of the fundamentals of mental disorder, we find, often to our discomfort, that almost any symptom can be produced by a gross organic lesion such as a tumor or by the most subtile psychological disturbance. No longer can we glibly state that because there is no intellectual deterioration, the problem is functional in origin. The use of electroencephalography and neuroradiology has become extremely valuable in the diagnosis of intracranial pathology which frequently manifests itself as representing functional disorders. Four cases are presented to demonstrate the value of these objective techniques as an aid to accurate diagnosis.

CASE REPORTS

Case 1: B. W. (fig. 1). This 35-year-old white female was admitted to Central Islip State Hospital 10/13/53. The family history revealed the father to be a heavy drinker. The patient lived with her mother and stepfather in a difficult emotionally unstable environment.

During adolescence the patient became shy, sensitive and developed antisocial tendencies which seemed to be self-limited. At the age of 19 Barbara married, and three children were born of this union.

One year prior to admission the patient developed unusual impulsive aggressive behavior with episodes of confusion. Two suicidal attempts are reported. She was admitted to a private mental hospital where she received a series of 10 electric shock treatments. After 8 weeks of hospitalization she was discharged with a diagnosis of schizophrenia, type simple.

Six months later the patient began feeling "nervous", became moody and irritable, lost interest in her housework, suffered fits of depression and complained of attacks of headaches, which resembled migraine. She started attending an out-patient psychiatric clinic where arrangements were made for psychoanalytic interviews. Because of the migraine-like attacks the possibility of an organic disease was suspected and an electroencephalogram requested. This showed electrical abnormalities compatible with those seen in convulsive disorders. Although this finding was associated with an episode of petit mal, no definite steps were taken to investigate the etiology of the condition. The patient's condition worsened, and at her own request she was admitted to the Central Islip State Hospital because of continued depression and fears that she might harm her children. The initial hospital examination revealed a depressed patient with, "flat affect and feelings of unreality." No positive neurological signs were detected. The patient related that she had been attending the clinic, and the electroencephalographic findings were available to the examining psychiatrist. Nevertheless a diagnosis of depressive state was made, and psychotherapeutic sessions were started. The diagnosis was later changed to psychoneurosis, mixed type, and it was not until the occurrence of a few attacks of petit mal and the observation of the paroxysmal character of the patient's behavioral disorder that the suspicion of an epileptic condition again arose. The electroencephalogram was repeated, and the findings were confirmatory of the previous records. A complete diagnostic workup was done. The cerebrospinal fluid examination was negative. The pneumoencephalogram did not reveal gross abnormalities. The left carotid showed that the multiple vascular arteriogram was normal, whereas the arteriogram of the right carotid showed multiple vascular malformations which were classified as arteriovenous racemose angiomas.

Under anti-convulsive medication the patient made a remarkable improvement and was discharged after a short time.

Comment: There are a few points in this case which deserve discussion. As far as the diagnosis is concerned, the importance of the attacks of migraine has to be recognized. In fact, these gave the first clue of any underlying organic cause. Had the attacks of petit mal

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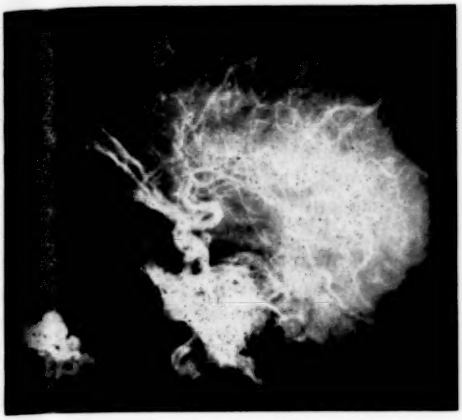

FIG. 1. *Case 1:* Left carotid arteriogram. Notice the simultaneous filling of arterial and venous vessels. The angiomatose malformations are noticeable in the frontal and in the frontal-temporal areas.

not been observed, it would certainly have been difficult to reach the diagnosis of epilepsy. Indeed the electroencephalographic findings, while compatible with the diagnosis of epilepsy, could also be seen in cases of migraine disorder. Retrospectively, it is hard to say how typical the psychiatric manifestations were to allow the diagnosis of epilepsy on purely clinical grounds, but it would seem that a finer appreciation of the state of confusion during episodes of impulsive aggressive behavior and the paroxysmal character of the disorder, plus the association of the attacks of migraine should have indicated an underlying organic dysfunction. Perhaps in the minds of some there would still be reservations in regard to the epileptic nature of the disorder if the workup had not been complete and if, by arteriography, organic lesions of the brain had not been demonstrated.

It is known that migraine is frequently caused by the presence of intracranial arterial malformations. Therefore it seems justifiable to relate the angiomas to the migrainous condition. It is more difficult to assess the intimate mechanism by which the vascular malformations produced the epileptic attacks, perhaps by simple mechanic action (compression, direct stimulation) or by alteration of the cerebral metabolism and the process of oxygenation in certain areas of the brain. The parallel improvement in the clinical manifestations and in the electroencephalographic record following anti-convulsive medication is significant.

Case 2: E. R. (fig. 2). This 30-year-old white female, mother of two children, was admitted to Bellevue Hospital, Psychiatric Division, 2/4/53. Her symptoms on admission were those of marked apathy and ideas of reference. She was transferred to Pilgrim State Hospital with the diagnosis of dementia praecox, simple type, where, on examination, she was found cooperative but evasive and dull; illogical and vague in her speech; partially oriented but with a lack of memory for recent and past events. No delusions and no hallucinations were elicited. The neurological examination was negative. The diagnosis of schizophrenia was maintained.

The course at the hospital was uneventful, but on 4/12/53 the patient felt dizzy and fell to the floor. In order to rule out a skull fracture x-rays of the skull were taken. No evidence of traumatic lesions was found, but the sella turcica appeared eroded and calcifications in the anterior fossa were visualized. The consulting neurosurgeon examined the patient and found an absence of sense of smell on both sides and active deep reflexes in the right arm. An intracranial tumor was suspected, and in order to verify the diagnosis a ventriculogram was attempted. Burr-holes were made in the frontal region anteriorly to the coronal suture, the dura was incised, and the cerebral cortex was exposed. The brain bulged through the trephine openings, and on passing the ventricular needles a resistance was felt on the left side. An incision was then made in the cerebral cortex and underlying white matter, and a hard tumor mass was visualized. The patient was then transferred to the Neurosurgical Service of the Psychiatric Division of Bellevue Hospital (7/9/53), where the following positive neurological signs were observed: broad-based gait, tendency to fall to the left, hyperactive reflexes on both sides, bilateral Babinski and initial papilledema bilaterally.

The lumbar puncture yielded clear, colorless cerebro-

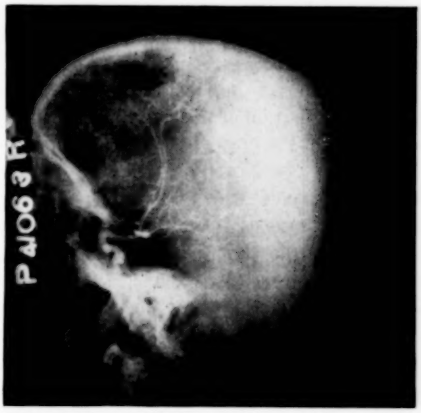

FIG. 2. *Case 2:* Right carotid arteriogram. Notice the characteristic displacement of the anterior cerebral artery and its branches. The syphon is pushed backwards and downwards.

spinal fluid under a pressure of 290 mm. of water. The protein content was 43 mg. per cent and 6 cells.

The electroencephalogram showed a focal slowing in the left anterior temporal region. The arteriograms of the left and right carotid demonstrated elevation and posterior displacement of the anterior cerebral arteries, strongly suggestive of a meningioma of the olfactory groove.

Under general anesthesia a frontal coronal flap was turned down, and a huge meningioma attached to the floor of the anterior fossa was visualized and totally removed. the post-operative course was uneventful, and the patient made a good recovery. The pathological report confirmed the diagnosis of meningioma.

There was also slow but steady improvement in the patient's mental condition, and it was possible to discharge her from the hospital.

Comment: Cases such as this do not represent rare experiences for neurosurgeons and psychiatrists. The chronicity of a slow growing intracranial tumor with its absence of objective or subjective symptoms is a common occurrence, and tumors situated in the so-called mute areas produce situations of this sort more frequently than others. The meningioma of the olfactory groove is the best known among these. It is this tumor which most often masquerades as a functional psychosis.

The only neurological sign which could be detected early in the course of the disease is the loss, unilaterally or bilaterally, of smell. It is indeed most unfortunate that many clinicians, in the routine neurological examinations, omit testing the state of function of the first cranial nerve. Although it is true that psychotics often lack the ability to cooperate adequately for accurate testing, an effort should always be made by the doctor to perform as complete an examination as possible.

Next in line of importance is the radiographic examination of the skull. Meningiomas in general and the ones of the olfactory groove in particular often produce evidence of their presence in ways which are detectable by means of x-rays (intramural calcifications, thickening of the tables, increase in vascular markings, sellar erosions, etc.). In this case the occurrence of the dizzy spell and the fall were most fortunate for the patient as they led to the suspicion of a skull fracture and the x-ray examination. Without that the course of events might have been different although a short time later many neurological signs were already present.

The best demonstration of the tumor, however, is obtained by arteriography, especially as there is a characteristic shift of the anterior cerebral arteries.

It is significant in this respect to emphasize that, once started, the progression of symptoms is quite rapid. Therefore the importance of an early diagnosis should be necessary. The recovery which this patient made represents a happy but unexpected outcome since extensive neurological signs and long term mental symptoms frequently indicate a poor prognosis.

Case 3: D. R. (fig. 3). This 36-year-old colored male was admitted to Central Islip State Hospital 10/19/50. The family history was essentially negative. The patient's physical development was apparently normal, but mentally he was somewhat retarded. He was not too bright at school and had no particular interests or aptitudes. At the age of 11 the patient suffered from a "sunstroke", remaining comatose for 3 weeks. He received supportive therapy and recovered "spontaneously". After he finished school, he worked at odd jobs but was never steadily employed. While in the Army the patient drank excessively and was AWOL frequently. Following his discharge he continued drinking heavily, consuming a quart or more of whiskey a day. Not infrequently he ran away from home for periods as long as a week. When drunk the patient did not become violent nor depressed. He saw "things" crawling on his bed and was afraid of them. In order to get money for his drinks he stole from members of his family and begged in the streets. Two years prior to admission to Central Islip State Hospital the patient was operated for appendicitis and supposedly was also treated for "a blood clot on the brain". He had also had several

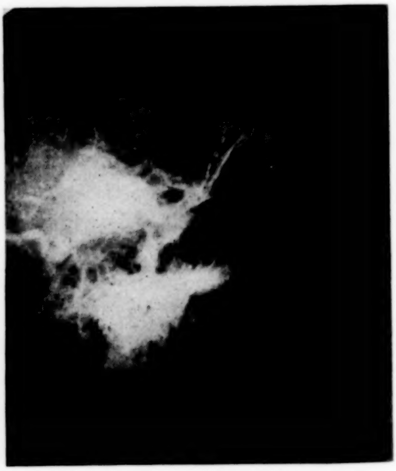

FIG. 3. *Case 3:* Left carotid arteriogram. The presence of a large arteriovenous malformation is evident.

previous admissions to other hospitals because of drinking. While in a state of acute alcoholism and suffering from visual hallucinations he was admitted to Bellevue Hospital, from which he was transferred to Central Islip State Hospital.

At the time of his admission the patient was found to be coherent and relevant but somewhat blunted and apathetic. He had visual hallucinations but was oriented in all spheres. With the diagnosis of psychosis due to alcohol, acute hallucinosis, the patient remained at the hospital for about 3 months and was then released on convalescence 1/15/51.

While at home the patient experienced severe headaches and had to be admitted for the second time 3 months later on 4/19/51. There were no essential changes in the patient's mental status. He hallucinated only sporadically and for short periods of time. This time, because of his blunted affect, he was diagnosed as schizophrenia, paranoid type.

In a short period of time the patient improved considerably, and discharge from the hospital was being contemplated when, on 2/7/52, an epileptic convulsion occurred. A workup was then started. The electroencephalogram showed abnormalities suggesting a focal pathology in the left temporal parietal area. The pneumoencephalogram, performed with a total amount of 120 cc. of air, demonstrated slight dilatation of the ventricular system. The left temporal horn appeared distinctly more dilated, and on the basis of this finding it was theorized that a lesion could be in the left hemisphere. A carotid arteriogram was therefore performed on the left side: A huge vascular malformation, located deep in the temporal lobe, was visualized. Under general anesthesia a large frontotemporoparietal flap was turned down, and the angioma was exposed and removed.

Post-operatively the patient was hemiplegic and aphasic but recovered promptly from the hemiplegia and to a certain extent from the aphasia. No significant changes were noted in the mental status.

Comment: The history and the clinical manifestations of chronic alcoholism were clear-cut in this case. There was nothing to indicate to the family or the physicians the possibility of a convulsive disorder. When the patient, during his second admission at the hospital, suffered a convulsion, it was difficult to assess its significance. Through the electroencephalographic findings it could be established that the patient was suffering from a focal intracranial disorder originating in the left temporal area. It was therefore possible that this was a case of psychomotor epilepsy. The question then was whether the alcoholism could be interpreted as disorder of behavior caused by the epileptic condition. Psychomotor epilepsy not infrequently manifests itself with disorders of character and behavior and often is due to focal lesions in the temporal lobe. The pathology is usually represented by gliosis, but in some cases lesions of another type, such as a tumor, have been found. In this case, by means of carotid arteriography, an arteriovenous malformation was demonstrated. Neurological examination did not indicate any physical abnormality. The anamnesis was also non-contributory in this respect, although retrospectively the "sunstroke" suffered by the patient many years before appears to have been an episode of intracranial bleeding.

The surgical intervention was successful in that it removed a potential source of hemorrhage although it did not improve the mental status of the patient.

Case 4: P. S. (fig. 4). A 64-year-old white male patient, admitted to Bellevue Hospital, Psychiatric Division, with a 5-year history of progressive mental deterioration and progressive speech difficulty.

Past history was essentially negative. Six years prior to admission the patient was "mugged" in the subway, and the following morning he appeared confused and somewhat unable to recall what had happened to him the night before. He recovered completely, however, and was well for about one year. He then became moody, irritable, slow in his responses, showed poor memory and difficulty in communicating with others.

At the time of admission the general physical examination was negative except for an enlarged, benign prostate. The neurological examination revealed a large left pupil reacting sluggishly to light; hyperactive deep

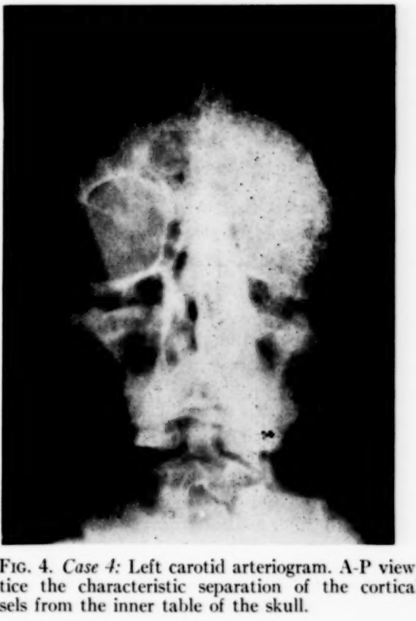

FIG. 4. *Case 4:* Left carotid arteriogram. A-P view. Notice the characteristic separation of the cortical vessels from the inner table of the skull.

reflexes; bilateral Hoffman sign (7); left Chaddock and left, inconstant Babinski. There were also signs of aphasia, echolalia, perseverance, delayed reaction and mental confusion. The impression was that the patient had organic lesion of the brain, possibly of a degenerative type.

In order to ascertain the nature of the process a series of diagnostic tests was done, and the following results were obtained: The electroencephalogram revealed abnormalities suggesting diffuse cerebral dysfunction without clear-cut indication of lateralization or focal pathology. The pneumoencephalogram, performed by injection of 100 cc. of air, showed symmetrical dilatation of the entire ventricular system without evidence of displacement. At the time the pneumoencephalogram was done and on one previous occasion, the cerebral spinal fluid was found xanthochromic but with a normal content of protein and under normal pressures. Carotid arteriograms were done. On the left, in the AP view, a depression of the cortical cerebral vessels characteristic of a subdural hematoma was seen.

The patient was then submitted to neurosurgery, and a large, chronic, subdural hematoma was found on the left side. The contents of the hematoma was represented by greenish fluid as the clot had undergone complete liquefaction. Two membranes, one internal and one external, were present. The latter presented itself thick but was easily separable from the inner aspect of the dura, whereas the internal membrane was comparatively thin and could be detached from the arachnoid with some difficulty. The underlying brain appeared markedly depressed, was not pulsating and did not re-expand upon evacuation of the hematoma.

Post-operatively an infection of the wound developed. The culture was positive for *Bacillus proteus*, *Staphylococcus aureus* and *Enterococcus*. It seemed at first that the infection could be controlled by topical and parenteral administration of the drugs to which the organisms were found to be sensitive, but, as later drainage started again, the removal of the bone flap was necessary. The infection, however, could never be controlled, and it extended to the left cerebral hemisphere. Death occurred after a short episode of respiratory failure.

Comment: In this case, since no history of head injury was obtained, a subdural hematoma was not suspected, and the clinical picture seemed to fit quite well with a degenerative process of vascular etiology. The first clue to a chronic subdural hematoma was given by the presence of what appeared to be xanthochromia in the spinal fluid. However, the content in protein was found to be normal and the pressure within normal limits. Thus the evidence became confused, and it was thought that the marked elevation in total protein was responsible for the xanthochromia. Moreover, the pneumoencephalogram and the electroencephalogram revealed no finding suggestive of a subdural hematoma. At this point, in the minds of many, perhaps, there would have been no further doubt of the process being of a simple degenerative nature. It was not until the arteriogram demonstrated abnormalities suggestive of subdural hematoma that the diagnosis could be made.

The operative findings gave an account of the xanthochromia found in the CSF. Apparently the yellow color was due to the presence of blood breakdown products which passed through the membrane and the arachnoid. In fact, at the time of the operation an intensely colored fluid was found between the inner membrane and the arachnoid.

In retrospect the midriasis associated with the defective response to light is significant, but it ought to be remembered that in cases of arteriosclerosis of the brain pupils of unqeual diameter are not a rare finding, so that the ocular signs *per se* could not be taken as symptomatic of subdural hematoma.

DISCUSSION

There are many reports in the literature which point to the fact that organic lesions of the brain can produce mental disorders of different types which, at times, do not differ significantly from those attributed to the functional mental disorders.

The peculiar clinical picture resulting from attacks of psychomotor epilepsy has been the object of interest by numerous authors.

Delay (3, 4), in particular, has commented on the fact that in some cases the epileptic manifestations closely resemble schizophrenia, depressive state, hysteria, obsessions and compulsions, and simple behavioral problems. This author has emphasized the difficulty that one encounters at times in differentiating between hysteria and epilepsy, as they can coexist in the same patient. The fact that emotional factors can be responsible for the occurrence of epileptic attacks is also considered.

The incidence of psychotic manifestations in cases of brain tumor has been mentioned by many authors. Although it is true that there is no statistical evidence pointing to a higher number of brain tumors among psychotics, intracranial space-taking lesions do not represent a rare accidental finding at autopsies in mental institutions. Of utmost interest to the psychiatrist are those cases in which no positive neurological signs are found and the symptomatology is restricted to manifestations of mental disorder. Recently Waggoner and Bagghi (11) reported a series of six such cases and emphasized the importance of electroencephalography for detecting focal cerebral lesions. Bruetsch (1) reported a case of meningioma of the olfactory groove which had not been suspected during the long period of time the patient had been observed and followed as a psychotic. Psychic disorders in subdural hematoma are not rare. Krayenbuhl (9) found in 75 per cent of his cases varied mental disturbances, such as defective retention, memory loss, slowness of thinking, affective disturbances, particularly euphoria with Witzelsucht, poor initiative and apathy. According to other authors (2, 6, 8, 10) the incidence of mental disorders in subdural hematoma is even higher, and DeMorsier (5) believes that they represent a constant finding. Not infrequently these are unassociated with physical findings of major or minor significance. It is usually in those cases in which psychiatric diagnoses are made that the hematoma may never be discovered. Neurological signs are often absent. When such signs are present, they are frequently atypical and so varied that the possibility of a subdural hematoma is overlooked. Usually the diagnosis of degenerative disease of the brain is made in such cases.

Although in our experience electroencephalography has proved itself of great diagnostic value, we wish to stress the point that, very often, only by performing a series of examinations can the disease be carefully evaluated and ultimately diagnosed. It is not unusual to have normal findings in a pneumoencephalogram and to be able to demonstrate, in the same subject, the pathology by arteriogram or *vice versa*. If the suspicion of an organic lesion in the brain has been formulated, it becomes almost imperative to carry out an adequate investigation. The risk that the tests imply is ordinarily small, provided that they are performed by those skilled in their application.

BIBLIOGRAPHY

1. Bruetsch, W. L.: Mental disorders arising from organic disease. In *The Biology of Mental Health and Disease*, pp. 302–326. New York: Hoeber, 1952.
2. Davidoff, L. M.: Mental symptoms among brain tumor patients, and brain tumors among insane. *N. Y. State J. Med., 30:* 1205, 1930.
3. Delay, J., Mailland, and Binois: Automatisme comitial et automatisme pithiatique. *Ann. medico-psychologiques, 101:* 500–505, 1943.
4. Delay, J.: Epilepsie psychiques et electroencephalographie. *Presse Med., 57:* 1037, 1949.
5. DeMorsier: Quoted by Krayenbuhl.
6. Henry, G. W.: Mental phenomena observed in cases of brain tumor. *Am. J. Psychiat., 12:* 415, 1932.
7. Hoffman, J. L.: Intracranial neoplasms; their incidence and mental manifestations. *Psychiat Quart., 11:* 561–575, 1937.
8. Kanzer, M.: Personality disorders with brain tumors. *Am. J. Psychiat., 97:* 812–830, 1941.
9. Krayenbuhl, M., and Noto, G. G.: *Das intrakranielle subdurale hematom.* Bern: H. Huber, 1949.
10. Strauss, I., and Keshner, M.: Mental symptoms in cases of tumor of the frontal lobe. *Arch. Neurol. & Psychiat., 33:* 986, 1935.
11. Waggoner, R. W., and Bagghi, B. K.: Initial masking of organic brain changes by psychic symptoms. *Am. J. Psychiat., 110:* 904–910, 1954.

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SPECIFIC TYPES OF ALPHA STREPTOCOCCI IN THE ETIOLOGY AND STREPTOCOCCAL THERMAL ANTIBODY IN DIAGNOSIS AND TREATMENT OF DIVERSE DISEASES

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It is the purpose of this paper to describe the methods used and report the results obtained in bacteriological studies on the etiology of diverse diseases, some of which are currently considered as due wholly to filtrable virus, some as of psychogenic origin, still others whose cause is unknown or erroneously considered as due to causes other than infection.

METHODS

The clinical diagnosis in persons studied was made by attending physicians in the usual manner from the clinical history, physical examination and the usual diagnostic laboratory procedures.

It was found in previous studies that both saprophytic and specifically virulent types of alpha streptococci are usually present in exudates of infection atria such as nasopharynx, tonsils, pulpless teeth and pyorrhea pockets. The virulent types of streptococci have been found to outgrow the non-virulent variants in serial dilution cultures in the highly favorable medium dextrose brain broth, in tall columns in test tubes, which affords a gradient of oxygen tension and other properties especially favorable for growth of respective specifically virulent alpha streptococci. All cultures were incubated at 35°C.

Separation of staphylococci, *E. coli* and saprophytic streptococci from the specifically virulent streptococci in nasopharyngeal swabbings was accomplished in serial dilution cultures in dextrose brain broth using a nicrome wire at steps of 10^{-2}, 10^{-6} and 10^{-10} in which the specifically virulent streptococci outgrow the avirulent streptococci, staphylococci and *E. coli* (1).

One milliliter of pure cultures of streptococci from nasopharyngeal swabbings from the end point of growth either at 10^{-6} or 10^{-10} of serial dilution cultures in dextrose brain broth was injected intravenously in a tail vein of white mice weighing from 15 to 20 grams. The inoculated mice, except a few that died, were etherized to death 20 to 24 hours following such injection.

Cultures were made by macerating comparable pieces from various organs and tissues with an iridectomy scissors in 1 ml. of dextrose brain broth in 4 ml. screw-capped vials. These inocula were rendered semisolid by the addition of 2.5 ml. of melted and cooled 0.75% agar in 0.2% dextrose. Colony counts were made after incubation at 35°C. for 24 hours. Comparable pieces of brain, heart, lung, liver, pancreas, kidney, spleen and testicle; knee joint, muscles and lymph glands approximately 5× the volume of the eye of the mouse, adrenals and ovaries were also cultured in this manner.

Since thermal antibody prepared from specific types of alpha streptococci elicits diagnostic cutaneous reactions on intradermal injection, it was thought that such thermal antibody solutions might agglutinate specifically the various strains of streptococci isolated in studies of the diverse diseases. Accordingly, the agglutinative action of thermal antibody solutions at five tenfold dilutions of 1–10 to 1–100,000 was determined for suspensions of respective streptococci containing approximately 4 billion per ml. by diluting dense glycerol-saturated NaCl suspensions of the streptococci, stored at 10°C. (2), isolated in studies of diverse diseases.

RESULTS OF INTRAVENOUS INJECTION INTO MICE OF STREPTOCOCCI ISOLATED FROM THE FOURTEEN GROUPS OF PERSONS HAVING DIVERSE DISEASES

Aside from the diagnoses of patients listed in table 1, the general health of the 35 males and 23 females studied was not greatly impaired.

Cultures were made from 14 different tissues or organs in each of 262 mice that had been injected intravenously 20 to 24 hours before with 1 ml. of the respective dextrose brain broth cultures of alpha streptococci from the

TABLE 1.—LOCALIZATION OF STREPTOCOCCI IN THE ORGANS OF MICE FOLLOWING INTRAVENOUS INJECTION OF DEXTROSE BRAIN BROTH CULTURES AS ISOLATED FROM THE NASOPHARYNX OF PERSONS HAVING WIDELY DIFFERENT DISEASES

Diagnosis in Persons From Whom the Streptococcus Injected Was Isolated	Cases	Mice Injected	Isolation of Streptococci in 0.5 ml. of 0.2% Dextrose 0.75% Agar from the Organs of Mice 20–24 Hours Following Intravenous Injection of Streptococci That Grew from the End Point of Growth of Serial Dilution Cultures in Dextrose Brain Broth from Nasopharyngeal Swabbings of Persons Having Widely Different Diseases												
			Eyes	Brain	Heart	Lungs	Ovaries or Testicles	Joints	Muscles	Lymph glands	Liver	Pancreas	Spleen	Adrenals	Kidneys
Glaucoma	2	8	155* 89	58 77	16 64	42 38	8 7	0			18 60	0	24 50	0	18 40
Chorioretinitis	2	12	98 82	60 58	18 50	12 40	6 9	45 18			50 76	5 3	38 68	10 10	19 50
Epilepsy	7	18	18 27	175 88	40 20	60 50	20 8	1 3			80 70	0	40 70	61 17	60 40
Schizophrenia	7	17	17 10	132 78	17 18	27 32	20 16	7 5			38 50	4 3	38 57	2 3	20 34
Multiple sclerosis	6	30	18 5	180 80	20 6	45 30	17 19	12 2			8 42	16 2	100 55	18 10	18 15
Epidemic poliomyelitis	5	21	3 1	190 82	84 58	80 50	0	38 38			80 50	0	62 46	0	80 38
Coronary heart disease	4	12	9 6	9 8	110 94	8 7	10 10	0			40 43	0	12 54	0	18 42
Respiratory infection	8	32	0	38 27	11 16	178 78	8 20	37 30			62 40	0	47 40	0	20 18
Infertility — Males	4	50	0	16 12	16 9	17 12	78 68 50 36	18 12			20 20	9 13	19 30	5 6	8 9
Infertility — Females	3	17	0	8 5	19 25	21 35	58 41 78 55	5 10			12 20	4 7	9 10	40 38	29 20
Arthritis	6	29	0	10 24	20 24	16 8	12 10	160 68			38 20	0	40 20	0	12 16
Myasthenia gravis	2	6	0	16 18	12 35	20 2	60 32	45 20	150 64		44 45	0	40 46	0	10 10
Muscular dystrophy	1	5	0	16 10	0	20 20	0	40 30	64 98		42 45	0	41 40	0	20 20
Infectious mononucleosis	1	5	0	5 2	5 2	80 60	4 5	5 4		130 98	10 20	8 5	60 28	7 5	10 30

* The upper figure in each instance indicates the average number of colonies isolated; the lower figure indicates the percentage of isolations of streptococci.

58 patients suffering from altogether 14 different disease entities. The average number of colonies that grew and the percentage incidence of isolations of streptococci from the different organs of mice following intravenous injection of pure cultures of streptococci from the end point of growth at 10^{-6} and sometimes at 10^{-10} of serial dilution cultures of nasopharyngeal swabbings are summarized in table 1.

It will be seen that the number of streptococci and the percentage incidence of isolations of streptococci from the different organs following intravenous injection were uniformly far greater from the organ of mice corresponding to the organ chiefly affected in the spontaneously occurring disease in persons from whom isolated than from the other organs. Thus the average number of 155 colonies of streptococci and the percentage incidence of isolations (89) from the eyes of mice following intravenous injection of the streptococcus isolated from the nasopharynx of persons having glaucoma were significantly greater than isolations from the other organs, and far greater than from eyes of mice similarly injected with streptococci from diseases other than of the eyes. The results in chorioretinitis were equally specific (3, 4). A similar truly remarkable elective or specific localization occurred in organs of mice corresponding to those chiefly involved in patients from whom the streptococcus was isolated from the nasopharynx in each of the 12 additional diseases studied. This was true alike in the case of diseases currently considered as due to infectious agents such as epidemic poliomyelitis (5), respiratory infections (6, 7, 8), arthritis (9, 10) and infectious mononucleosis as well as in diseases of unknown etiology and currently not generally considered as due to infection such as glaucoma, chorioretinitis, epilepsy (11), schizophrenia (11), multiple sclerosis (12), coronary heart disease, infertility in otherwise well male and female persons, myasthenia gravis (13) and muscular dystrophy.

The number of colonies of streptococci and the percentage incidence of isolations of streptococci from the brain of mice that had received intravenous injection of the streptococcus from the nasopharynx of persons having diseases of the nervous system, idiopathic epilepsy (175; 88%), schizophrenia (132; 78%), multiple sclerosis (180; 80%), and epidemic poliomyelitis (190; 82%) were fairly comparable and far greater than isolations from any of the other organs of mice that received these "neurotropic" streptococci and far greater than isolations from the brain of mice receiving the streptococcus isolated from the nasopharynx of persons having diseases other than of the nervous system. The relatively high incidence (84; 58%) of isolation of streptococci from the heart of the mice injected with the streptococcus from epidemic poliomyelitis is in accord with the usual abnormal increase in the pulse rate and to the occasional sudden death from cardiac failure in the acute phase of epidemic poliomyelitis.

Isolations of streptococci (110; 94%) from the heart of 12 mice inoculated with alpha streptococci isolated from the nasopharynx of 2 cases of coronary heart disease and from the thrombosed coronary artery after death of 2 additional cases were far greater than from any of the other organs receiving comparable injections and far greater than isolations of streptococci from the heart of mice receiving similar injections of streptococci from persons not having coronary heart disease.

The isolation of the streptococcus from the lungs of mice that had been injected with the streptococcus isolated in studies of respiratory infection (178; 78%) was far greater than following similar injection of streptococci from other sources except injections of streptococci from infectious mononucleosis (80; 60%), a disease which usually follows attacks of respiratory infection.

Three childless married couples and one other married man, all in good health, ranging from 25 to 32 years in age who desired children were studied from the standpoint of the possibility that a specific symptomless streptococcal infection or intoxication having predilection for the reproductive organs, the testicle in the male and ovary in the female, might conceivably be responsible for such infertility. In the case of the female sex, such a possibility was indicated years ago when pure cultures of alpha type streptococci were isolated from surgically removed cystic ovaries of infertile excessively nervous married women. These streptococci were shown to have predilection for the ovary of rabbits on intravenous injection (14).

Each of 7 persons, 4 males and 3 females, studied in the infertile group was pronounced normal physically by their respective urologists and gynecologists. The motility of spermatazoa in the semen of the males was found deficient. All 7 persons appeared and felt well at the time of my study. The streptococci that grew from the nasopharyngeal swabbings at the end point of growth in serial dilution cultures in dextrose brain broth were injected intravenously into altogether 67 mice in the usual manner (table 1). The mice remained apparently well and as in the other groups were etherized to death 20 to 24 hours after the respective injections. Cultures of testicle and ovary of the inoculated mice yielded pure cultures of the streptococcus in far higher numbers and incidence than did the other organs following injection of the streptococci from both infertile males and females. The isolations of streptococci from the testicle of mice following injection of the streptococcus from infertile males (68; 36%) were somewhat higher than isolations following injection of streptococci from infertile females (41; 55%). Isolations from ovary were somewhat greater following injection of the streptococci from the infertile males (78; 50%) than following injection of streptococci from infertile females (58; 78%). Isolations from other organs in the infertility group were minimal throughout. Moreover, isolations of streptococci from the testicle or ovary of mice receiving the streptococcus from sources other than the infertile group (with but one exception—myasthenia gravis) were far less than in mice receiving corresponding injections of streptococci from the infertile group.

Isolations of streptococci from the joints of mice (160; 68%) injected with the streptococcus from the nasopharynx of arthritics were far greater than isolations from joints of mice receiving comparable injections of streptoccci from the nasopharynx of persons not having arthritis. Localization in muscles was very high following injection of the streptococci isolated in studies of myasthenia gravis (150; 64%) and in muscular dystrophy (64; 98%). Likewise streptococci were isolated in large numbers and high incidence (130; 98%) from the lymph glands following injection of strepto-

TABLE 2.—LOSS OF ORIGINAL SPECIFICITY AND A PHENOMENAL ACQUISITION OF BROAD LOCALIZING PROPERTIES OF SPECIFIC TYPES OF ALPHA STREPTOCOCCI AS ISOLATED IN STUDIES OF DIVERSE DISEASES ON PROLONGED STORAGE (71 DAYS AT 10°C.) OF A MIXTURE OF 14 SUCH SPECIFIC STRAINS IN DENSE SUSPENSION OF THE GLYCERIN-SATURATED NACL SOLUTION MENSTRUUM

Material Injected Intravenously in Mice			Mice Injected	Average Number of Colonies and the Percentage Incidence of Isolation of Streptococci from Organs of Mice 24 Hours After Intravenous Injection of Dextrose Brain Broth Cultures of the Streptococci											
				Eyes	Brain	Heart	Lungs	Liver	Pancreas	Spleen	Adrenals	Kidneys	Ovaries	Testicles	Joints
One ml. of dextrose brain broth cultures of streptococci from	Glycerin-NaCl solution suspension diluted 10^{-2} and 10^{-8} into male mice		9	160* 100	90 87	430 87	370 87	750 100	420 100	760 100	340 100	450 100		120 76	300 48
	Single colony on blood agar plate of the stored gly.-NaCl solution suspension into females		9	170 90	40 50	220 80	430 100	640 80	680 100	340 100	680 100	520 90	325 100		500 80
	Glycerin-NaCl solution suspension at dilutions of	10^{-2}	8	40 50	120 75	280 100	600 100	400 100	380 100	770 100	520 100	380 100	or 210 75		180 75
		10^{-8}	8	30 50	160 75	250 78	340 100	400 76	300 100	680 100	600 100	400 100	180 100		160 78
	Single colony on blood agar plate of the stored glycerol-NaCl solution suspension		8	50 78	100 50	270 78	380 78	280 100	270 100	680 100	680 100	300 78	140 50		120 50

* The upper figure in each instance indicates the average number of colonies; the lower figure indicates the percentage incidence of isolations.

cocci isolated in studies of infectious mononucleosis (80; 60%) which usually follows respiratory infections.

The number of colonies and percentage incidence of isolation of the streptococcus from the liver, spleen and kidney without evidence of lesions were uniformly high regardless of the source of the streptococcus, indicating it would seem a protective scavenger-like function of these organs. Streptococci were isolated in small numbers also without evident lesions from the pancreas and adrenals.

Streptococci were not isolated from any of the organs of 12 uninoculated control mice that were etherized to death except for a small number of streptococci from the lungs of one mouse. Moreover, cultures made of an additional group of 10 normal mice (not shown in the tables), etherized to death 24 hours after intravenous injection of 1 ml. of sterile NaCl solution, were also free from streptococci.

A truly remarkable change in localizing properties of the streptococci that grew in dextrose brain broth from the composite mixture in glycerin-NaCl solution of the 14 respective specific strains occurred during storage at 10°C. for 71 days (table 2). The specificities or elective localizations characteristic of the respective specific strains had disappeared. In addition to the expected somewhat broader localization following intravenous injection of subcultures in dextrose brain broth from the stored mixture of specific strains, the number of streptococci and the percentage incidence of isolations from the different organs of mice were almost without exception far greater than what would be expected if the streptococci so stored had not acquired far broader localizing and survival properties or virulence. Moreover, since such broad change in localization occurred following the intravenous injection of dextrose brain broth cultures of the streptococcus that grew from inoculations of the composite suspension diluted 10^{-2} and most importantly at 10^{-8} and from single colonies that grew on blood agar, it follows that each streptococcus that remained viable in the stored composite glycerin-NaCl solution suspension had acquired the diverse localizing properties characteristic of the 14 respective specific strains.

This remarkable increase in localizing property or "virulence" recalls the results of experiments made years ago in which non-virulent pneumococci acquired virulence by exposing them to sterile NaCl solution extracts ("virulin") of highly virulent pneumococci (15).

A similar phenomenal increase in total and broader localization on storage of a mixture of streptococci having different specificities has been observed in other similar experiments. Most remarkable of all are the facts 1) that the changes in the composite mixture of the respective specific types of streptococci occurred at a temperature of 10°C. and other conditions that precluded growth, 2) that the newly acquired properties were transmissible as the streptococci grew in subculture in the dextrose brain broth, and 3) that such changes never occurred under comparable conditions of storage of specific strains separately. In fact, storage separately of dense suspensions of respective specific strains in non-toxic glycerol-saturated NaCl solution resulting in dehydration of the streptococci in this liquid non-toxic menstruum has been used successfully for years in my studies to maintain viability, original virulence and antigenic specificity of alpha streptococci as isolated in studies of diverse diseases. The ability to prove specificity of non-hemolytic or alpha streptococci as isolated in studies of diverse diseases is due in large part to the use of glycerin-NaCl suspensions.

DIAGNOSTIC CUTANEOUS REACTIONS INDICATING SPECIFICITY OF STREPTOCOCCI

The marked specificity of erythematous cutaneous reactions for 6 widely different diseases is shown in table 3. The immediate erythematous cutaneous reactions to homologous natural and thermal antibody were uniformly far greater than the reactions in controls in each of the six widely different diseases studied.

Specificity of the cutaneous reactions on intradermal injection of thermal antibody prepared from streptococci isolated in studies of 14 widely different disease entities is strikingly shown in table 4. The cutaneous reactions were uniformly far greater in persons ill with the respective diseases from which the streptococcus was isolated and from which the thermal antibody was prepared, than reactions in persons ill with unrelated diseases and than in well persons.

SPECIFICITY OF ALPHA STREPTOCOCCI AS INDICATED BY AGGLUTINATIVE TITERS OF RESPECTIVE THERMAL ANTIBODY SOLUTIONS

The agglutinative titer of thermal antibody prepared from streptococci isolated in studies of the 14 disease entities for homologous and heterologous streptococci is shown in table 5. The agglutinative titer of the respective antibody solutions was uniformly far greater for homologous than for heterologous strains of the streptococci. The parallelism in the different diseases studied between the cutaneous reactions to intradermal injection of antibody solutions, and their agglutinative titers for the

TABLE 3.—DIAGNOSTIC CUTANEOUS ERYTHEMATOUS REACTIONS TO INTRADERMAL INJECTION OF THE EUGLOBULIN FRACTION OF THE SERUM OF HORSES THAT HAD BEEN IMMUNIZED WITH STREPTOCOCCI AND THERMAL ANTIBODY PREPARED BY AUTOCLAVING NaCl SOLUTION SUSPENSIONS OF THE RESPECTIVE STREPTOCOCCI

Diseases	Type of Antibody Injected Intradermally	Erythematous Cutaneous Reactions (sq. cm.) Following Intradermal Injection of Natural and Thermal Antibody Prepared Respectively from Streptococci Isolated in Studies of					
		Respiratory infection	Poliomyelitis	Encephalitis	Arthritis	Epilepsy	Schizophrenia
Respiratory infection	Natural	256* $\boxed{10.42}$	46 1.76	37 2.20	45 2.3		
	Thermal	263 $\boxed{11.04}$			185 2.13		
Poliomyelitis	Natural	53 3.21	484 $\boxed{8.97}$	268 3.30	270 2.41		
	Thermal		254 $\boxed{14.21}$	15 4.21	23 2.45		
Encephalitis	Natural	91 3.06	54 3.27	138 $\boxed{6.88}$	50 180		
	Thermal			25 $\boxed{9.23}$	20 2.21		
Arthritis	Natural		85 1.50	85 2.00	87 $\boxed{8.12}$		
	Thermal			19 3.47	104 $\boxed{9.63}$		
Epilepsy	Natural				41 1.97	41 $\boxed{8.11}$	41 3.37
	Thermal				41 2.45	41 $\boxed{9.63}$	41 5.15
Schizophrenia	Natural				89 1.42	89 3.51	89 $\boxed{5.66}$
	Thermal				89 1.93	89 4.51	89 $\boxed{7.49}$

* The first figures in each instance indicate the number of persons tested; the second figures indicate the average reaction in square centimeters. Squared figures indicate specificity.

TABLE 4.—DIAGNOSTIC ERYTHEMATOUS CUTANEOUS REACTIONS IN DIVERSE DISEASES FOLLOWING INTRADERMAL INJECTION OF HOMOLOGOUS STREPTOCOCCAL THERMAL ANTIBODY

Source of Streptococci	Erythematous Cutaneous Reactions (sq. cm.) Following Intradermal Injection of Thermal Antibody Prepared from Streptococci Isolated from the Nasopharynx of Persons Having:													
	Schizophrenia	Epilepsy	Multiple scler.	Encephalitis	Poliomyelitis	Respiratory infec.	Arthritis	Coronary ht. disease	Muscular dystrophy	Myasthenia gravis	Leukemia	Infertility	Alcoholism	Migraine & Men. dis.
Schizophrenia	414* $\boxed{9.08}$	414 5.62		34 4.57			414 2.24							
Epilepsy	450 5.24	450 $\boxed{10.71}$					450 2.24							
Multiple sclerosis			47 $\boxed{13.29}$	6 4.12		20 3.25	22 3.22							
Poliomyelitis				115 4.21	602 $\boxed{11.50}$	95 4.24	224 1.90							
Respiratory infection				75 4.20		572 $\boxed{12.03}$	336 2.14							
Arthritis	118 3.30	118 3.40		19 3.43			118 $\boxed{11.57}$							
Coronary heart disease						6 4.64	7 3.70	12 $\boxed{15.44}$	9 1.88					
Muscular dystrophy							2 11.39		4 $\boxed{14.21}$	2 12.50				
Myasthenia gravis							4 4.42			4 $\boxed{16.79}$				
Leukemia						3 4.25	4 4.43				6 $\boxed{9.79}$			
Infertility						5 9.01	2 9.83					5 $\boxed{13.30}$		
Alcoholism	19 3.14					14 3.73	7 4.99						21 $\boxed{14.09}$	
Migraine				2 3.34		8 5.80	8 4.36							18 $\boxed{13.33}$
Well persons	236 1.74	236 1.53		379 1.54	127 1.20	455 3.87	236 1.85							

* The first figures in each instance indicate the number of persons tested; the second figures indicate the average reaction in square centimeters and the squared figures indicate specificity.

respective streptococci indicating specificity were truly remarkable.

RESULTS IN TREATMENT WITH RESPECTIVE NATURAL AND THERMAL STREPTOCOCCAL ANTIBODY

Diminution in cutaneous reactions indicating specific circulating streptococcal antigen and increase in reactions indicating circulating antibody occurred on repeat intradermal injection of antibody and antigen, respectively. Clinical improvement followed therapeutic intramuscular injection of respective natural or thermal antibody solutions in these and previous studies in the treatment of epidemic poliomyelitis (16, 17) influenza and other respira-

TABLE 5.—SPECIFIC AGGLUTINATION IN PER CENT OF ALPHA STREPTOCOCCI AS ISOLATED IN STUDIES OF DIVERSE DISEASES BY THE HOMOLOGOUS THERMAL ANTIBODY SOLUTIONS

Thermal Antibody Prepared from Streptococci Isolated in Studies of	Pool Number and Strains per Pool From Which Thermal Antibody Was Prepared	Agglutination of Streptococci in Per Cent by Thermal Streptococcal Antibody at Five Tenfold Dilutions of 1-10 to 1-100,000 as Isolated in Studies Respectively of													
		Schizophrenia	Epilepsy	Multiple scler.	Encephalitis	Epidemic poliomyelitis	Resp. inf.	Arthritis	Cor. heart disease	Muscular dystrophy	Myasthenia gravis	Leukemia	Infertility	Alcoholism	Migraine & Meniere's
		(14)*	(15)	(19)	(6)	(14)	(26)	(13)	(8)	(4)	(16)	(6)	(7)	(6)	(14)
Schizophrenia	9702-12	$\boxed{45}$	10	35	25	20	25	10	40	0	0	0	10	0	0
Epilepsy	9704-15	10	$\boxed{40}$	30	0	10	10	20	30	25	15	15	15	20	5
Multiple sclerosis	9708-19	5	15	$\boxed{65}$	0	30	15	25	55	20	0	10	5	0	0
Encephalitis	9721-6	25	0	35	$\boxed{55}$	35	35	40	30	35	40	25	15	10	10
Poliomyelitis	9711-14	0	5	50	15	$\boxed{60}$	35	0	55	25	0	30	20	40	0
Respiratory infection	9706-10	0	5	35	15	25	$\boxed{45}$	25	25	30	30	20	10	20	0
Arthritis	9722-6	0	0	15	15	20	25	$\boxed{50}$	45	25	30	15	15	25	15
Coronary heart disease	9712-7	10	10	30	10	15	30	0	$\boxed{75}$	25	15	25	10	25	30
Muscular dystrophy	9714-4	0	0	20	35	30	20	35	40	$\boxed{65}$	40	25	34	20	20
Myasthenia gravis	9716-16	0	0	0	25	20	20	25	20	35	$\boxed{55}$	15	15	25	20
Leukemia	9719-5	0	0	10	10	15	10	0	15	15	20	$\boxed{45}$	15	25	20
Infertility	9715-4	0	5	5	20	0	10	10	20	0	10	15	$\boxed{50}$	10	15
Alcoholism	9717-4	0	10	0	25	5	0	30	20	15	15	25	15	$\boxed{45}$	20
Migraine & Menier's Dis.	9720-12	5	10	35	10	35	20	30	35	20	25	20	20	20	$\boxed{50}$

* Figures in parentheses indicate number of strains of streptococci subjected to agglutinations.

tory infections (8, 18), idiopathic epilepsy and schizophrenia (19), epidemic encephalitis (20 21), epidemic hiccup (22), compulsive behavior of criminals (23), streptococcus viridans endocarditis (24) and chronic ulcerative colitis (25).

Summary and Comments

The number of streptococci and percentage incidence of isolations from 14 different organs of mice 20 to 24 hours after intravenous injection of dextrose brain broth cultures of alpha streptococci as isolated from the nasopharynx of 58 persons having widely different diseases whose etiology was either wholly obscure or due to infection are reported. There was little or no evidence of a faulty inheritance, occupational predisposition or dietary deficiencies in the different groups of patients.

The streptococci isolated in pure cultures from the end point of growth of serial dilution cultures in dextrose brain broth and which localized specifically in mice following intravenous injection were without exception of the non-hemolytic or alpha type.

In keeping with the fairly normal general health except in poliomyelitis and respiratory infections and the specific ailment of the patients from whom isolated, the streptococci on isolation had a low general virulence but an exceedingly high affinity for the respective organs or tissues of mice corresponding to the ones affected in the patients from whom isolated.

The number of streptococci and the percentage incidence of isolations from the organs of the inoculated mice corresponding to the ones affected in the respective patients were uniformly far greater than from organs not affected except from the lesion-free liver, spleen and kidney representing perhaps a scavenger-like function of these important massive organs. Causal relationship of the streptococci isolated from the nasopharynx in the diverse diseases studied is indicated 1) by their localizing maximally in the organs of mice on intravenous injection corresponding to the respective tissues or organs chiefly affected in patients from whom isolated, 2) by the diagnostic erythematous cutaneous reactions on intradermal injection of the respective streptococcal thermal antibody solutions, and 3) by the specific agglutination of the respective streptococci by the corresponding streptococcal thermal antibody.

The question whether the respective streptococci which are culturally and morphologically much alike represent separate, unrelated strains from extraneous sources such as food, water or air or whether the respective specificities represent acquired properties of the alpha type streptococci normally present in the nasopharynx of human beings is uncertain. However, judging by the results of experiments on the transmutation of the streptococcus-pneumococcus group (13) in which marked changes in localizing properties occurred in "pure line" strains on repeat animal passage and loss of such specificity on cultivation in unfavorable mediums, it is likely that the respective specificities of the streptococci in these naturally-occurring diseases are acquired or develop in the respective hosts. Since the conditions in some of the patients had persisted for several years and the general health was not greatly impaired, it almost seems that the persons ill with such chronic localized diseases supply the very physicochemical or other conditions under which the indigenous streptococci normally present in the throat of human beings acquire and maintain respective specific organotropic properties.

The maintenance almost indefinitely of respective specificities on storage separately of specific strains of alpha streptococci as partially dehydrated in the glycerol-NaCl solution menstruum (table 1) and the phenomenal increase in organotropic localization on additional identical storage of composite mixtures of respective specific strains of streptococci (table 2) is new, truly remarkable and fundamental, for it indicates the importance of environmental conditions for the acquisition and maintenance of respective specificities of the ever-present alpha streptococci in human beings. The importance of determining specificities inherent or acquired of alpha type streptococci in studies on etiology such as these is obvious.

BIBLIOGRAPHY

1. Rosenow, E. C.: Elective localization of streptococci. *J. A. M. A., 65:* 1687–1691, 1915.
2. Rosenow, E. C.: Diagnostic cutaneous reactions to intradermal injection of natural and artificial

antibody and of antigen prepared from streptococci isolated in studies of diverse diseases. *Ann. Allergy, 6:* 485–496, 1948.

3. Rosenow, E. C.: Iritis and other ocular lesions on intravenous injection of streptococci. *J. Infect. Dis., 17:* 403–408, 1915.
4. Rosenow, E. C., and Nickel, A. C.: Elective localization in determining the etiology of chronic uveitis. *Am. J. Ophthalmol., 15:* 1–18, 1932.
5. Rosenow, E. C., Towne, E. B., and Wheeler, G. W.: The etiology of epidemic poliomyelitis. Preliminary note. *J. A. M. A., 67:* 1202–1205, 1916.
6. Rosenow, E. C.: Studies on the etiologic relation of streptococci to acute epidemic respiratory infections. *Am. J. Clin. Path., 15:* 319–333, 1945.
7. Rosenow, E. C.: Studies on the relation of pneumotropic streptococci to influenza virus. *Am. J. Clin. Path., 15:* 362–380, 1945.
8. Rosenow, E. C.: Nonhemolytic streptococci in relation to an epidemic of influenza. Diagnostic cutaneous tests and specific treatment. *A. M. A. Arch. Otolaryngology, 54:* 609–619, 1951.
9. Rosenow, E. C.: The etiology of articular and muscular rheumatism. *J. A. M. A., 60:* 1223–1224, 1913.
10. Rosenow, E. C.: The newer bacteriology of various infections as determined by special methods. *J. A. M. A., 63:* 903–907, 1914.
11. Rosenow, E. C.: Bacteriologic, etiologic and serologic studies in epilepsy and schizophrenia, I. *Postgraduate Med., 2:* 346–357, 1947.
12. Rosenow, E. C.: Bacteriological studies of multiple sclerosis. *Ann. Allergy, 6:* 271–292, 1948.
13. Rosenow, E. C., and Heilman, F. R.: Bacteriologic studies in myasthenia gravis. *Proc. Soc. Exper. Biol. & Med., 34:* 419–425, 1936.
14. Rosenow, E. C., and Davis, C. H.: The bacteriology and experimental production of ovaritis. *J. A. M. A., 66:* 1175–1180, 1916.
15. Rosenow, E. C.: Transmutations within the streptococcus-pneumococcus group. *J. Infect. Dis., 14:* 1–32, 1914.
16. Rosenow, E. C.: Specific streptococcal antigen and thermal antibody in the prevention, diagnosis and treatment of epidemic poliomyelitis. *South Dakota J. Med. & Pharmacy, 5:* 304–310, 328, 1953.
17. Rosenow, E. C.: Relation of a streptococcus to epidemic poliomyelitis. Studies in etiology, diagnosis and specific treatment. *California Med., 76:* 396–401, 1952.
18. Rosenow, E. C.: Diagnostic cutaneous reactions, specific prevention and treatment in epidemic respiratory infections. *Arch. Otolaryngology, 58:* 609–622, 1953.
19. Rosenow, E. C.: Bacteriologic, etiologic and serologic studies in epilepsy and schizophrenia. III. Cutaneous reactions to intradermal injection of streptococcal antibody and antigen. *Postgraduate Med., 3:* 367–376, 1948.
20. Rosenow, E. C.: Specific serum treatment of epidemic (lethargic) encephalitis. Further results. *J. A. M. A., 80:* 1583–1588, 1923.
21. Rosenow, E. C.: Epidemic encephalitis in North Dakota and Minnesota, 1941: Studies on etiology, epidemiology and serum treatment. *Lancet, 63:* 247–257, 1943 (with H. W. Caldwell).
22. Rosenow, E. C.: Etiology and serum treatment of persistent epidemic and post-operative hiccup. *J. Lab. & Clin. Med., 28:* 277–289, 1942.
23. Rosenow, E. C.: Influence of streptococcal infections on the compulsive behavior of criminals. *Postgraduate Med., 10:* 423–432, 1951.
24. Rosenow, E. C.: Immunological studies in chronic pneumococcus endocarditis. *J. Infect. Dis., 7:* 429–456, 1910.
25. Rosenow, E. C.: Serum treatment for chronic ulcerative colitis. *Arch. Int. Med., 46:* 1039–1047, 1930 (with J. A. Bargen and G. F. Fasting).

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PSYCHOPATHOLOGICAL ACCOMPANIMENTS OF CHRONIC RELAPSING PANCREATITIS

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In 1945 Rickles (9) suggested the possibility that psychological factors might enter into the total picture of pancreatic disease. Williams (13) reviewed this suggestion and concluded that occasional anxiety symptoms were extraneous and were often a confounding factor leading to the improper diagnosis of psychophysiological gastrointestinal reaction. He cited one case in which anxiety and paranoid symptoms were manifest, but which psychological testing showed to be normal. Savage, Butcher, and Noble (11) noted the presence of alcoholism and emotional difficulties in a high percentage of 60 chronic and acute pancreatitis cases, but they gave limited information on the kind of difficulty observed. McCleery, Kesterson and Schaffarzick (4), in a report on vagotomy of 11 cases, again offered the general statement, without data, that all cases showed some degree of emotional inadequacy. In addition, they stated that they considered chronic recurrent pancreatitis to be of psychogenic origin, and that their cases correspond to the "ulcer personality" as described by diverse authors. A. Phillips (6) and R. Phillips (8) concur in their observation of both alcoholism and emotional disturbance. The present study is an attempt to demonstrate in objective terms the existence of psychopathology in a group of these patients, as well as to explore possible patterns of psychodynamics.

PROCEDURE

Twenty white male veterans were seen during a period of about a year. All were thoroughly studied and given the diagnosis of chronic relapsing pancreatitis by the medical staff. They were extensively interviewed and tested in times of remission between attacks of pancreatitis. Though all the patients were cooperative, the fact that some of them did not consider themselves emotionally disturbed probably led to an underestimation of the amount of psychopathology in some of the measures used. The mean age of the group was 47.6 years, ranging from 30 to 65, and the mean educational level was 9.7, ranging from two years of grammar school to a law school graduate.

Three psychological tests were administered: 1) The Minnesota Multiphasic Personality Inventory (MMPI), a 550-item questionnaire giving exhaustive coverage of emotional symptoms and attitudes; 2) the Cornell Medical Index, a 195-item questionnaire covering a wide range of physical symptoms, as well as emotional symptoms; 3) the Rorschach Inkblot Test, a projective psychological test designed to give information which might not be available from consciously expressed attitudes.

INTERVIEW DATA

Thirteen of the 20 patients have at one time or another been hospitalized in the neuropsychiatric service of VA hospitals, and of these, 10 were diagnosed as suffering from a psychiatric disability prior to receiving the diagnosis of chronic pancreatitis. Examination of their records revealed that most of such diagnoses appeared to have been based upon behavior deviations and emotional symptoms rather than somatic symptoms which might have been confused with the symptoms of pancreatitis.

In giving their life histories, a great many of these patients appeared to be defensive and anxious to paint a picture of their early family lives as being near-perfect. In only three cases did there seem to be a realistic evaluation of both positive and negative qualities of parents. In the case of seven patients there was disruption of the home prior to adolescence by either death or divorce of the parents. Closer examination of patients' descriptions of their parents revealed, however, two outstanding configurations. In 12 cases the mother was described as protective but strict on discipline, forceful, and generally domineering. ("She had a mind of her own;" "she was good-hearted, but pretty strict".) In these cases, the patients found it harder to describe their fathers, and the impression was given that they counted for less in the home, left the raising of the children up to the mother, and were easygoing, passive individuals. On the other hand, for six of the patients, the description of the mother was vague but suggestive of indifference, while the father either was openly described as harsh and punishing, or was considered as "too strict at times". The other two patients were raised in orphanages.

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Such a family constellation in either instance would suggest difficulty in establishing proper identification with a masculine figure. Either the combination of male and female roles seen in the domineering mother or the isolation resulting from the punishing father would be most conducive to feelings of inadequacy, irresponsibility, and persistence of unsatisfied dependency needs.

Reflection of these traits may be found in these patients' subsequent life history data. Perhaps the most striking illustration may be found in their psychosexual adjustment. Table 1 shows their present marital status. Ten patients have been divorced one or more times, while two are single. Six of the divorced patients (30 per cent of the entire group) are at present not remarried. This proportion may be compared with 1950 national census data listing about 4 per cent of urban white males aged 30-65 whose marital status is divorced (14) (chi-square test gives a probability <.001). This rate exceeds by far even the number of divorced alcoholics (12 per cent) as reported by Schneyer (12). Of the 12 now married, seven have known difficulty with their spouses. Seven patients admit sexual difficulty, mainly impotence and promiscuity. Including divorce, present marital difficulty, and impotence or promiscuity, 17 of the 20 show evidence of psychosexual maladjustment.

TABLE 1.—MARITAL STATUS

Married, never divorced	8	
Known marital difficulty		5
Married, previously divorced	4	
Known present marital difficulty		2
Divorced	6	
Single	2	

TABLE 2.—OCCUPATIONAL STATUS

Occupational Classification	Highest Occupational Achievement	Occupational Status during Past Year
Professional	3	0
Skilled worker	7	2
Independent businessman	6	0
Semiskilled worker	2	2
Laborer	2	4
Unemployed	—	10
Retired	—	1

Examination of the patients' vocational histories offers further evidence for the existence of psychopathology. Table 2 shows a comparison of early adult vocational attainment with vocational level for the year prior to their being seen for this study. Originally they consisted of three professionals, six independent businessmen, seven skilled workers, two semiskilled workers and two laborers. Although many of them had manifest personality disturbances at the time, apparently they were able in spite of their disturbance to achieve above-average vocational status. At the present time, however, of the 19 who are still of working age, only eight have been able to earn their own living during the past year. Three of the eight who are still working do not work steadily, and two others are working at jobs considerably below their previous level. It is difficult to evaluate the extent to which physical illness has handicapped some of these patients, but even in the few with whom this is clearly a factor, it is probable that emotional health would have enabled them at least to compensate partially for their periodic attacks of pancreatitis.

Alcoholism has been noted as a concomitant of pancreatitis in most studies of this illness. Table 3 shows the incidence of alcoholism in this group. Use of alcohol was admitted by all but two patients, while two patients, being given the benefit of the doubt, appeared to drink only moderately. Classification of the other 16 as heavy drinkers was based upon their own admission, Army and VA records, and occasionally upon statements by relatives. Ten of these heavy drinkers had had two or more episodes of acute alcoholic hallucinosis. It is of interest to note that the two nondrinkers were the only ones in the group who

TABLE 3.—INCIDENCE OF ALCOHOLISM

Non-drinkers	2	
Moderate or questionable drinkers	2	
Heavy drinkers	16	
Acute hallucinosis episodes		10

have had manifest psychotic disturbances. One was hospitalized for 20 months with a diagnosis of involutional depression, but he had made a good home and occupational adjustment for several years at the time of the study. The other had not been hospitalized but was an obvious ambulatory schizophrenic, experiencing auditory hallucinations, ideas of reference and persecutory delusions. Although generalization is impossible where there is such a low frequency of occurrence of psychosis, it is of interest to speculate upon whether the use of alcohol serves as a defense mechanism against the development of psychosis.

The operation of dependency needs can thus be seen in the difficulty accepting responsibility that is indicated by marital trouble, occupational decline, and alcoholism. Clinical evaluation of the patients gives surface impressions of two distinct kinds of people. Roughly half of the group tended to be overtly passive, anxious for support from others, and in spite of their outward submissiveness unable to avoid unconscious antagonism toward other people, thus jeopardizing their dependency relationships. The other patients showed outward pseudo-aggressiveness mainly in the form of demands that they be taken care of by others or complaints about how inadequate their care was. For both groups the dynamics appear to be equivalent: unsatisfied dependency needs leading to passive-aggressive behavior which results in their being rejected and thus confirming the original feeling of inadequacy. There was rarely evidence for strong attempts to deny dependency needs on any but the most conscious verbal level at the time the patients were seen. Some of their early occupational attainments suggested a period of more active striving but a later giving in completely to passive-aggressive behavior. Since all of these patients were chronically ill, it is probable that the rationalization that the illness provided removed the final barriers against full acting out of their dependency needs.

Fifteen of the group readily admitted to being "nervous", but in all but three instances this nervousness was viewed as an affliction imposed upon them externally, either by illness or through the hostility of other people. Only three of the twenty were able to conceive of intrapsychic emotional distrubance in which they themselves played a major role.

The most common complaints were of generalized muscular tension and somatic preoccupation even in times of remission from attacks of pancreatitis. There was a noticeable scarcity of intropunitive neurotic complaints. While feelings of hopelessness and depression were common, the causes for these complaints tended to be sought in situations and people external to the patient himself. Twelve patients had bothersome ideas of reference, though only one showed this to psychotic proportions.

In this exploratory study no systematic attempt was made to investigate possible relationship between emotional state and outbreak of acute attacks of pancreatitis. Several striking instances were noted, however, thus suggesting an area for future investigation. As an example, one patient, interviewed during a 2-month remission of symptoms, described his early years in an orphanage and his feelings of loneliness, and remarked that he had not thought of these experiences for a long time. That night typical symptoms of an acute attack of pancreatitis occurred, confirmed by the usual laboratory findings.

Since most of these patients were admitted for short periods of time, and many were unwilling to go into a great deal of detail about their past lives, it is impossible to attempt any greater specificity in characterizing the psychogenesis of their conflicts. Three cases will be summarized to illustrate the type of individual encountered.

Case 1: Age 55. Patient was the third of four children, the only boy in the family. His father made a good living as a jewelry designer, but his work was sometimes unsteady because of his drinking. He was a strict disciplinarian and would beat the patient at times or keep him up all night as punishment. He also was harsh and abusive toward patient's mother and sisters. The mother could endure this treatment silently, but when her children were grown, she finally divorced patient's father. In spite of this environment, patient feels that he got along reasonably well. He was happy with his contemporaries and was looked after, especially by his sisters, to whom he is still closely attached. He quit school at 13 to help his mother and enlisted in the Army at 18 for two years of uneventful service. He had no interest in girls at this time. His wife, whom he married when he was 29, was the first girl who had seriously interested him and also the first girl with whom he had sexual relations. They were divorced after five years. Patient sees the cause for their difficulties in her extravagance with money, her liking "a good time" and finally in her going out with other men. He could think of no way in which he contributed to the difficulty, and blames the beginning of his drinking upon his wife's infidelity. After his divorce, patient lived with his mother and sisters for about 15 years, then married again. This second wife was apparently psychotic (eventually hospitalized with a paranoid psychosis), and the marriage lasted only two years. Patient had several jobs as a dispatcher in the trucking business, one of which he held for 21 years, but he felt that he was always discriminated against because he was "the sucker who would do all the work." After he left this job, he had six different positions lasting for shorter and shorter times. Patient was either fired "for no reason" or suddenly quit when he felt he was being taken advantage of. In the past four years the patient has not worked and has obtained financial help from his sisters. The local employment service reports that he has refused many jobs because he felt they were "beneath him". He expressed an interest in receiving psychotherapy, but during a 6-week hospitalization was unable to go beyond blaming others for his condition. The onset of chronic relapsing pancreatitis came shortly after his second marriage. For the past seven years his symptoms have made him uncomfortable, but he required hospitalization only twice during acute episodes. It is clear that his emotional adjustment was poor many years prior to the development of pancreatitis and that his illness has not been so severe as to cause total unemployment for four years.

Case 2: Age 49. Patient is the second of two children, though he was virtually an only child because of the death of his older brother. His parents ran a prosperous real estate business. The father was "easygoing, placid, and scrupulously honest, so that people took advantage of him." His mother "had definite ideas of right and wrong, and had the business head, a very efficient woman." Patient wanted to be a commercial artist, but due to parental pressure attended college. He enrolled in three different institutions but stayed less than one semester at each. He always had a reason for quitting, such as "In Kansas they were all six feet tall and didn't have any use for me." Patient had many sales jobs and at least five businesses of his own, all of which failed, leaving his family with the bills to pay for him. Patient married when he was 34 and obtained an annulment nine months later. He blames this failure on his wife's dislike of sexual relations, refusal to have children, and her antagonism to patient's mother. He says it was at this time that he began to get nervous, though he admitted drinking heavily for many years previously. Another business failed at this point. He became convinced that his lawyer was trying to cheat him, and instituted disbarment proceedings. He also later tried to disbar two other lawyers involved in the settlement of his father's estate. After his Army service, he again had another business failure, then spent several years disposing of the family estate. For the past five years he has been employed as a sign painter but has been missing more and more time from his job because of illness and drinking. Three years ago he married a friend of his first wife, who is apparently quite domineering. Recently this marriage has been threatened by patient's drinking and undue demands. Pancreatitis symptoms occurred four years ago. He has had three short hospitalizations for it, with less severe symptoms every three or four months. On his last admission he had recovered from an acute attack, but almost immediately after he was informed that he was to be discharged, his symptoms reappeared, subsiding a few days later after it was decided to transfer him to the psychiatric service. Patient readily agreed that he was nervous and felt that he should be treated for "a nerve in my neck that got twisted when I was injured overseas." He talked readily in psychotherapy about his countless somatic symptoms and the injustices that had befallen him, but always felt misunderstood when his own role in his troubles was pointed out to him.

Case 3: Age 42. Patient is the fourth of 11 children, whose father did not work at all during most of patient's life. The father claimed he was sick, but patient said that no doctor was ever able to find anything wrong with him physically. He would sit alone doing nothing and showing little interest in the family while patient's mother was out earning a living. Patient said of his mother "she would sometimes holler, but since the kids did most of the housework, she didn't complain." This was virtually the only thing patient had to say about his mother. She was interviewed and found to be affectionately interested in patient, but quite aggressive. She told of instances when patient would cry about his condition, and she told him to "start acting like a man." Patient was described as being always obedient and anxious to help people, but tending to rely on his older sisters too much. Patient felt that childhood and adolescence were always happy, and he considered himself sociable, carefree and even-tempered. He began driving trucks as soon as he could get a license and has done this ever since. He was married at age 28 to a girl whom he describes as "a nice girl who would do anything to help you, but she's a little nervous." They were separated in their second year of marriage because of "arguments over little things," but were reunited within a short time. Patient's mother feels that the wife has endured more from him than she herself would have. In the Army patient developed peptic ulcer and became nervous while in combat zones. He was given a medical discharge. He and his family agree that he "changed completely" while in the service, to an irritable, withdrawn person. He has worked sporadically since then, having had eight or nine jobs since discharge. His family has often been on relief and has received much help from patient's sisters. Since his discharge he has had little interest in sex. He had a subtotal gastrectomy four years ago and around that time had his first attack of pancreatitis. He has had four hospital admissions since then, twice developing an acute hallucinatory psychosis after admission. He admits having been a heavy drinker in the past but denies drinking anything but beer in the past two years. This patient was excessively passive and obsequious in manner, though he complained mildly about the various physical and psychological tests he was asked to do. He complained of having many crying spells, periods of irritability, lack of energy, and self-consciousness. He readily saw himself as the cause of his financial troubles, but felt that everything would be all right if he could be relieved of his "stomach trouble".

PSYCHOLOGICAL TEST RESULTS

Confirmation of some of the clinical observations was sought in data from the psychological tests. It was hoped, first, that the existence of psychopathology could be demonstrated, and second, that data relevant to the dynamics of the patients could be found. Suitable measures were not readily available for some of the traits, such as strength of dependency needs. In addition, the absence of a matched control group makes it necessary that these results be viewed as tentative.

Eleven MMPI scales were used. Table 4 shows the mean scores of the pancreatitis group, together with the approximate range of normal scores (mean ± one sigma, approximately). The means of three scales lie in the pathological range: Hypochondriasis, Depression, and Ego Strength. The means of four scales lie in a range higher than is reported for normal groups but which is not definitely pathological: Hysteria, Psychopathic Deviate, Psychasthenia, and Hypomania. The means of four scales are near the normal range: Paranoia, Schizophrenia, Dependency and Manifest Anxiety.

The Cornell Medical Index indicates that the pancreatitis patients check a significantly higher number of items relating to emotional symptoms than a group of 20 non-psychosomatic medical and surgical patients of the same age (chi-square test gives a probability <.05). The pancreatitis patients also checked a higher total number of items than did the non-pancreatitis patients, but the difference was not statistically significant (table 4).

Analysis of the Rorschach was limited to consideration of five previously validated indices. Table 4 shows the mean scores for these variables as reported by various investigators. The anxiety content mean was less than the reported normal level, while the hostility content mean exceeded that reported for normals. The percentage of good form responses (F + %) was in the normal range, suggesting that these patients perceive in a reality-bound manner. Scoring for quality of location choice indicates a genetically immature approach to the whole responses, while the detail response is approached in a normal manner.

TABLE 4.—PSYCHOLOGICAL TEST DATA

	Pancreatitis Patients' Mean	Approximate Normal Range
Minnesota Multiphasic		
Hypochondriasis	71.6	40–59
Depression	74.0	40–59
Hysteria	64.3	40–59
Psychopathic deviate	64.4	40–59
Paranoia	54.8	40–59
Psychasthenia	61.3	40–59
Schizophrenia	59.5	40–59
Hypomania	60.3	40–59
Manifest anxiety	19.6	8–24(10)*
Ego strength	38.6	45–57(1)
Dependency	22.3	11–27(5) Twenty normals
Cornell Medical Index		
Total items checked (median)	33.0	27.5 (not significant)
Emotional symptoms checked (median)	5.3	.91(p <.05) Reported normal mean value
Rorschach		
Elizur anxiety score	3.2	5.2(3)
Elizur hostility score	3.9	1.3(3)
Good form responses per cent (F + %)	87.6%	79%(2)
Genetically high whole responses	69.8%	83%(7)
Genetically high detail responses	82.1%	76%(7)

* Numbers in parens refer to bibliography.

The test results clearly confirm the existence of emotional symptoms in this group. Depressive feelings, overconcern with body processes, low level of integration, and to a lesser extent, a tendency toward acting out of conflicts are typical of the group. In addition, the low level of anxiety and the high hostility are consistent with their clinically-noted denial of emotional conflict and tendency to project their problems onto other people and situations. On the other hand, the most outstanding dynamic trait observed in the interviews, dependency needs, failed to be demonstrated by the MMPI. It is believed that this is due to an inadequacy of the scale itself, which was derived in an *a priori* fashion and not validated against an external criterion of strength of dependency need. Nevertheless, it is clear that further research is necessary to demonstrate objectively that such a need is central in people with this illness.

SUMMARY

Twenty patients with chronic relapsing pancreatitis were studied by means of interview and psychological tests. A high incidence of psychosexual maladjustment, occupational inefficiency and alcoholism was noted. Although many patients were vague in their description of early family life, it was observed that they tended either to describe the mothers as dominant or the father as severe and punishing. It is suggested that these parental attitudes led to feelings of masculine insufficiency, irresponsibility, dependence and passive-aggressive behavioral patterns which were reflected in their later lives. The Minnesota Multiphasic, the Cornell Medical Index, and the Rorschach test confirmed the existence of psychopathology in these patients. Somatic preoccupation, depression, and behavioral symptoms were characteristic, while psychotic traits and manifest anxiety were not evident. They tended to show a higher than normal hostility level, but the clinically-noted dependency strivings failed to be confirmed by the particular measure chosen.

BIBLIOGRAPHY

1. Barron, F.: An ego strength scale which predicts response to psychotherapy. *J. Consult. Psychol., 17:* 327, 1953.
2. Beck, S. J., Rabin, A. I., Thiesen, W. G., Molish, H., and Thetford, W. N.: The normal personality as projected in the Rorschach test. *J. Psychol., 30:* 241, 1950.
3. Elizur, A.: Content analysis of the Rorschach with regard to anxiety and hostility. *Rorschach Res. Exch., 13:* 247, 1949.
4. McCleery, R. S., Kesterson, T. E., and Schaffarzick, W. R.: A clinical study of the effect of vagotomy on recurrent acute pancreatitis. *Surgery, 30:* 130, 1951.
5. Navran, L.: A rationally derived MMPI scale to measure dependency. *J. Consult. Psychol., 18:* 192, 1954.
6. Phillips, A. M.: Chronic pancreatitis—pathogenesis and clinical features. *Arch. Int. Med., 93:* 337, 1954.
7. Phillips, L., and Smith, J. G.: *Rorschach Interpretation: Advanced Technique.* New York: Grune and Stratton, 1953.
8. Phillips, R. W.: Study of gastric secretory levels in chronic relapsing pancreatitis. Paper presented to the New England Veterans Administration Clinical Research Society, Sturbridge, Mass., Oct. 1, 1954.
9. Rickles, N. K.: Functional symptoms as first evidence of pancreatic disease. *J. Nerv. & Ment. Dis., 101:* 566, 1945.
10. Sampson, H., and Bindra, D.: "Manifest" anxiety, neurotic anxiety, and the rate of conditioning. *J. Abnorm. & Soc. Psychol., 49:* 256, 1954.
11. Savage, C., Butcher, W., and Noble, D.: Psychological manifestations in pancreatic disease. *J. Clin. & Exper. Psychopathol., 13:* 9, 1952.
12. Schneyer, S.: The marital status of alcoholics. *Quart. J. Studies Alc., 15:* 325, 1954.
13. Williams, R. D.: Chronic pancreatitis. *Am. J. Med., 7:* 137, 1949.
14. *World Almanac, 1954.* New York: New York World-Telegram and Sun, 1954.

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THE SIGNIFICANCE OF CHARACTERISTIC AUTONOMIC NERVOUS SYSTEM RESPONSES IN THE ADJUSTMENT, CHANGE AND OUTCOME IN SCHIZOPHRENIA

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Introduction

Investigations of autonomic nervous system processes in their relationship to the schizophrenic process have primarily dealt with the efficiency of organs that are responsible for the secretions of the substances adrenin and acetylcholine.

Hoagland (16) has shown that, in a study of one hundred schizophrenics, two-thirds of this group was subnormal in its adrenocortical output. Pincus *et al.* (24, 25), in a series of studies, show that hypo-activity of the adrenal cortex is found when subjecting a group of disturbed subjects to situations involving a sudden threat to the organism. Confirmation of this finding comes from a similar type research study of Hoagland (16), who likewise finds fairly consistent hypo-active adrenocortical responsivity in situations of psychological stress. Freeman and co-workers (8, 9) suggest that the schizophrenic reaches a stable balance at the cost of losing contact with his environment. The behavioral picture of the schizophrenic emerges as being non-discriminating, non-adaptive, and inflexible. This state is likewise reflected in the schizophrenic's autonomic nervous system sluggishness, as indicated by defective adrenocortical functioning.

Release of adrenalin from the medulla of the adrenal gland, activated by hypothalamic activity, results in effects associated with sympathetic discharge. Fibers associated with the parasympathetic system release acetylcholine which has effects similar to parasympathetic enervation. Release of this substance has effects similar to those produced by electrically stimulating the medial and anterior nuclei of the hypothalamus. If we regard schizophrenia as a disease process in which communication between the individual and his environment has become disrupted, it leads one to suspect that the mechanism whose function it is to cope with such sensations would likewise reflect such an impairment. Investigating the extent of such impairment may then become an indicator of not only the present state of adjustment but also may have important prognostic implications.

Funkenstein *et al.* (11, 12, 13, 14) have shown that a significant relationship exists in a group of mentally ill patients between the reaction to the injection of autonomic nervous system stimulants and the reaction to electric shock therapy (ECT) and insulin coma therapy (ICT). Results of blood pressure changes after the injection of a parasympathetic stimulant, mecholyl chloride, and a sympathetic stimulant, epinephrine hypochloride, were used as indicators. A number of investigations have attempted to discover relationships between physiologically induced autonomic nervous system reactions, psychological test findings, and progress of the schizophrenic disorder after, or before, ECT and ICT (7, 21, 22).

The importance of a study designed to investigate the relationship between autonomic reaction patterns and spontaneous improvement rests upon its possible consequent predictive value regarding outcome of illness. It has largely become standard procedure to utilize shock and drug treatment techniques upon hospitalization of a schizophrenic patient. The effects of such techniques, while beneficial in some cases, are relatively uncontrolled and not fully understood. Patients giving a favorable autonomic response to the Funkenstein test (11) would conceivably be spared from the possible undesirable side effects of uncontrolled treatments.

Statement of Problem

This study was an attempt to relate observed behavioral adjustment of institutionalized schizophrenic patients to blood pressure changes following the injection of the adrenergic drug "epinephrine hypochloride" and the cholinergic drug "mecholyl chloride". Furthermore it is an attempt to relate observed behavioral changes observed over a 2 months time span to characteristic blood pressure changes following injection of the drugs. As Funkenstein, Greenblatt, and Solomon (14) have indicated, success or failure of ECT and ICT can be significantly predicted on the basis of characteristic blood pressure reactions to the adrenergic drug mecholyl chloride. The objective of this particular study rests upon the need to possess a clinical tool that can be used as a possible prognostic instrument to predict whether or not a patient suffering from a schizophrenic break will recover without the interference of shock treatments. Shock treatment may be regarded as possessing chiefly an ameliorative value, especially when viewed as a tool to calm the disturbed patient or to elevate the mood of the depressed patient. The choice between the use of barbiturates and shock treatment in calming the patient has become in many instances a highly arbitrary one. It is no exaggeration to state that in many state hospital settings use of ECT and ICT has become a standard procedure. The indiscriminate use of such treatment appears to be highly undesirable as a general policy since neither improvement nor failure to improve after shock treatment can be explained or accurately predicted. While it is quite true that shock treatments frequently do have beneficial effects, it appears highly desirable to this investigator to predict a patient's behavioral adjustment more accurately before subjecting him to a series of shocks.

The problem may be stated in the following hypotheses:

1) The quality of behavioral adjustment in schizophrenics is significantly related to a characteristic autonomic nervous system reaction as defined by the direction of blood pressure change, induced by the cholinergic drug mecholyl chloride. a) Decrease of blood pressure following the injection of mecholyl chloride is related to favorable behavioral adjustment. b) Increase of blood pressure following the injection of mecholyl chloride is related to unfavorable behavioral adjustment.

2) The quality of behavioral adjustment in schizophrenics is significantly related to a characteristic autonomic nervous system reaction as defined by the direction of blood pressure change, induced by the adrenergic drug epinephrine hypochloride. a) Decrease of blood pressure following the injection of epinephrine hypochloride is related to unfavorable adjustment. b) Increase of blood pressure following the injection of epinephrine hypochloride is related to favorable behavioral adjustment.

3) The trend of spontaneous behavioral adjustment changes over an 8-week observation period in schizophrenics is significantly related to the direction of blood pressure changes following the injection of mecholyl chloride. a) Decrease of blood pressure is related to a favorable behavioral adjustment change over an 8-week observation period.

4) Discharge from the Traverse City State Hospital is significantly related to blood pressure changes following the injection of mecholyl chloride. a) Decrease of blood pressure is related to hospital discharge within a 5-month period after admission of a group of schizophrenic patients to the state hospital.

METHODOLOGY

Selection of the subjects

The subjects selected for this study consisted of 60 patients, diagnosed unequivocally as suffering from a schizophrenic disorder. These subjects were obtained at the Traverse City State Hospital. Care was taken to utilize only patients free from the following disorders: heart disease, thyroid disorder, tuberculosis, diabetes, hypertension, or any organic disorder involving central or peripheral nerve mechanisms. Inasmuch as the drugs epinephrine and mecholyl chloride constitute some threat to the organism when administered, it was felt that any complication arising from using the drugs would be minimized in this manner.

The age range of the subjects extended from age 19 to 41 years, with a mean of 28.7.

One of the objectives in this study was to investigate spontaneous behavior changes over a 2-month time span in patients suffering from schizophrenia, without the administration of any of the physical therapies. This proved to be one of the most difficult aspects to control. While ICT was not difficult to control since it was not administered during the time of study, ECT was administered as standard procedure. The original sample of 87 patients was reduced to a total of 60, primarily due to the administration of ECT at some time during the observation period. None of the patients received any psychotherapy during the time of this study. Some of the patients did receive hydrotherapy. It was not felt that the effects of this therapy have any more far-reaching effects than the general environmental change that occurs when a patient is admitted to the hospital surroundings.

The original aim had been to utilize a sample of patients totally comprised of recent first admissions to the receiving hospital. However, sample controls as described above necessitated the use of a sample of schizophrenic patients who had been institutionalized for a period not exceeding three years. While the majority of subjects had been institutionalized less than one year (70%), none of the subjects used had received any ECT. The sample thus includes subacute as well as acute schizophrenics. Care was taken to include only subjects who had not previously been institutionalized. This was deemed to be important since frequently the record accompanying the patient neglects to include possible therapy the patient might have obtained.

Although the sex of the patient did not appear to have any bearing on the results of the study, it developed by chance that the population of 60 was divided evenly into 30 males and 30 females.

Procedure in the administration of drugs

The drugs, epinephrine hypochloride, a synthetic equivalent of the adrenergic hormone adrenaline, and mecholyl chloride, the synthetic equivalent of acetylcholine, were administered to all 60 subjects. A dosage of .05 mg. of epinephrine hypochloride was administered according to Funkenstein (11). Prior to the intravenous injection of the drug, the subject was subjected to an intravenous injection of saline solution, in order to control the possible psychological effects which may cause great fluctuations in blood pressure. Any subject fluctuating more than 10 points from his resting blood pressure was eliminated from the sample.

After each patient had recovered from the epinephrine hypochloride injection, as indicated by blood pressure return to normal, mecholyl chloride was administered intramuscularly. A dosage of 10 mg. of mecholyl chloride was administered following Funkenstein (11). It is to be noted that this procedure differs from Funkenstein's, insofar as the mecholyl chloride injections were administered on the same day as the epinephrine hypochloride injections. This was done in an effort to avoid the considerable upset of patients when they are transferred to different surroundings, required in order to administer the drugs. The fact that mecholyl chloride was administered after basal blood pressure measures had been obtained for a minimum of 5 minutes indicates that the injections of epinephrine hypochloride had been neutralized by the organism.

Procedure in the evaluation of blood pressure changes

The critical aspect of this study involved the accuracy of blood pressure measurements prior to, during, and following the administration of the drugs. The instrument used was the reliable arm cuff manometer. Great care was taken to instruct student nurse personnel in the accurate measurement of blood pressure since careless use of the measuring instrument could seriously impair the accuracy of readings. According to Funkenstein, only systolic readings were recorded (11). Speed and accuracy of measurement were of prime importance in the evaluation of extremely rapid blood pressure changes.

At the beginning of the experiment, patients were kept in a supine position for a minimum of 15 minutes. During this time, a minimum of three blood pressure readings were obtained. Following this resting period, the saline solution was administered, and an additional three blood pressure readings were obtained. Out of this minimum total of six readings, average systolic pressure was obtained. After the administration of epinephrine hypochloride, blood pressure readings were obtained every 15 seconds for a period of 7 minutes.

After blood pressure had returned to normal, usually within a 15-minute period, the drug, mecholyl chloride, was administered. Blood pressure readings were obtained every 30 seconds for a period of 6 minutes, followed by readings every 60 seconds, until a total of 25 minutes had elapsed since injection time. During both epinephrine hypochloride and mecholyl chloride reactions, blood pressure readings were stopped when a subject yielded a minimum of three readings in succession of equal pressure.

Using normal blood pressure as a base line, increases and decreases of blood pressure were carefully recorded. The maximum amounts of blood pressure increase and of blood pressure decrease were used as the critical figures in this study.

Procedure in the evaluation of behavioral adjustment

The instrument used in the evaluation of behavioral adjustment and of changes in behavioral adjustment was the Gardner Behavior Chart (29). This chart was developed as an aid in obtaining such a record in the patients' behavior, so as to allow a running commentary on behavioral adjustment as well as changes in adjustment. The following categories are used in determining behavioral adjustment: attention to personal appearance, sleep, appetite, sociability, activity control, care of property, self-entertainment, cooperation on routine, work capacity, work initiative when alone, work initiative when supervised, willingness to follow directions. Under each category five brief phrases characterize the degree of adjustment for the specific behavior segment. The numerical evaluation for these five phrases runs from 0—none, 1—poor, 2—fair, 3—good, and 4—extra good. In this manner, a possible maximum mean score of four and a possible minimum mean score of zero can be obtained.

The Gardner Behavior Chart appears to be well-suited for behavioral evaluations. It utilizes a number of questions designed to elicit direct information that appears to be inherently valid since these questions deal concretely with those aspects of behavior that demand a direct answer. The wording of the questions appears to be of such a nature as to allow little if any misconception on the part of nurses and attendants who supply the information. In a study of post-operative changes in a group of lobotomized patients, the Gardner Behavior Chart was used extensively. Schrader and Robinson (27) point out that these scores make possible the quantitative consideration of group averages, as well as affording convenient indices for judging the status of individual patients. In their particular study, it was of great value inasmuch as it significantly indicated critical differences between pre- and post-operative scores.

Patients in the sample were rated twice weekly for a period of 8 weeks. Each weekly rating was obtained twice on the same day from two different shifts of nurses and attendants. This was done for the following reasons: 1) that practical circumstances required different attendants and nurses due to frequent shift in personnel; 2) that possible halo and anchoring effects were avoided; and 3) that double ratings could be used in a reliability estimation of the instrument. Observation over a period of 8 weeks was felt to be a minimum in order to discover any trends of behavioral change in the group of patients.

Procedure in the evaluation of hospital status five months after investigation

The 60 patients were classified as to status 5 months after the drug injections. This classification was as follows: paroled from hospital, in hospital, indeterminate status (such as home visit or family care). Only the first two groups were used in the evaluation of status and its relationship to drug reactions. These first categories represent clearly definable status and were used in the evaluation. In this manner, 51 subjects could be used in this investigation.

Results with epinephrine hypochloride

It had been predicted that significant relationships could be obtained between good behavioral adjustment and an increase of blood pressure after the administration of epinephrine hypochloride. Conversely, it was predicted that a significant relationship could be obtained between poor behavioral adjustment and a fall in blood pressure following the administration of epinephrine hypochloride. The concepts of "good" and "poor" behavioral adjustment are a function of the relative standing of the Gardner Behavior Chart mean score for each patient. A maximum "good"

TABLE 1.—PEARSON r CORRELATIONS BETWEEN BLOOD PRESSURE CHANGES AS A FUNCTION OF EPINEPHRINE HYPOCHLORIDE AND MECHOLYL CHLORIDE INJECTIONS AND GARDNER BEHAVIOR CHART MEAN SCORES FOR SIXTY SCHIZOPHRENIC PATIENTS

N = 60	Gardner Behavior Chart Mean Scores	
Blood pressure rise after epinephrine injection	r S.E. r	.13* .115
Blood pressure fall after epinephrine injection	r S.E. r	.06* .128
Blood pressure rise after mecholyl injection	r S.E. r	−.53† .094
Blood pressure fall after mecholyl injection	r S.E. r	.43† .107

* Correlation non-significant.

† Correlation significant at the one per cent level or less.

adjustment would be reflected by a mean score of four and a maximum "poor" adjustment by a mean score of zero. In other words, "good" and "poor" indicate high and low scores on the Gardner Behavior Chart and are a function of the total sample used in this investigation.

Using Pearson r coefficients in order to investigate these predictions, no significant relationship could be established (table 1). One cannot distinguish between a favorable and an unfavorable adjustment on the part of schizophrenic patients when the drug epinephrine hypochloride is used. Blood pressure changes as a result of the use of this drug will not discriminate between patients on the basis of their behavioral adjustment. This is in partial agreement with Funkenstein's findings (11), in which he stresses the point that only a subjective evaluation of anxiety could be used as a dependable criterion for differential reactions to the drug epinephrine hypochloride.

Results with mecholyl chloride

The hypothesis formulated predicted that a significant relationship could be established between good behavioral adjustment and a fall in blood pressure after the administration of mecholyl chloride. Conversely, the hypothesis had predicted that an increase in blood pressure after the administration of mecholyl chloride would be significantly related to poor behavioral adjustment.

Using Pearson r coefficients in order to investigate these two hypotheses, significant relationships were established (table 1). This leads one to the conclusion that the reaction a schizophrenic patient will manifest following the injection of mecholyl chloride is of considerable prognostic importance. Blood pressure changes as a result of injection of this drug will significantly discriminate between patients on the basis of their behavioral adjustment.

Results with mecholyl chloride in an investigation concerned with behavior changes

The hypothesis had been advanced that trends of behavioral improvement over an 8-week time span will be significantly related to the blood pressure reaction to mecholyl chloride. It had been predicted that maximum blood pressure fall would significantly relate to significant behavioral improvement as shown by a rise in behavior ratings during the 8-week observation period. Conversely, maximum blood pressure rise would significantly relate to behavioral deterioration as reflected by a fall in behavior ratings during the 8-week observation period. Analysis of the significance of difference of behavioral rating means between the first and the eighth week of observation revealed the following: For the group of 15 patients who had shown maximum rises of blood pressure following the injection of the cholinergic drug mecholyl chloride, a significant difference between behavior rating means for the first week of observation and for the eighth week of observation could be established. The significance of this difference between behavior rating means occurs in the direction of decrement. This difference is significant at below the .01 level of confidence in the direction of behavioral deterioration (table 2). For the 15 patients who showed a maximum fall of blood pressure following the injection of mecholyl chloride, analysis of the significance of difference between first and eighth week behavior rating means revealed significance at the .05 level of confidence in the direction of behavioral improvement (table 2). These findings support the hypothesis: Behavioral deterioration over an 8-week time

TABLE 2.—Tests for the Significance of Difference of Gardner Behavior Chart Means between the First and the Eighth Week of Observation, for the Fifteen Subjects Having Largest Increases and the Fifteen Subjects Having Largest Decreases of Blood Pressure Following Mecholyl Chloride Injection

Group N = 15	Gardner Behavior Chart		
	Mean	*Mean difference*	*t*
Blood pressure increase			
First week	1.95		
Eighth week	1.68	.27	3.068*
Blood pressure decrease			
First week	2.54		
Eighth week	2.74	.20	1.818†

* Significant at below the one per cent level.

† Significant at the five per cent level.

span is significantly related to maximum blood pressure rise following the injection of mecholyl chloride in a group of 15 patients who evidenced maximum blood pressure increase out of a total group of 60 schizophrenic patients. Fall in blood pressure after the administration of mecholyl chloride is significantly related to behavioral improvement over an eight week time span, in a group of fifteen patients that evidenced maximum blood pressure fall out of a total group of sixty schizophrenic patients (table 2).

Results with mecholyl chloride in an investigation concerned with patient status five months after drug injection

The object of this follow-up study was to determine whether blood pressure reactions to the injection of mecholyl chloride could be related to the future status of patients at the hospital. The patient was considered cured if he had been returned to his home; he was considered institutionalized if still at the hospital 5 months after the initial experiment. Out of the group of 60 patients, 51 were either paroled to their home or were still institutionalized. The remaining nine patients were of an indeterminate status, due to their placement in family care or temporary home visit. A Chi square analysis showed a significant relationship between greater fall than rise in blood pressure after the injection of mecholyl chloride, and release from the hospital within 5 months after the initial experiment. Conversely, a larger rise than fall of blood pressure could be related to continuing hospitalization 5 months after the initial investigation. These findings were significant at the one to two per cent levels of confidence (table 3).

TABLE 3.—Chi Square Analysis of Release or Institutionalization Five Months after the Initial Investigation, and Blood Pressure Reactions following the Administration of Mecholyl Chloride

	Blood Pressure Increase	Blood Pressure Decrease
Release	5	14
Institutionalization	20	12
		·H 51

$\chi^2 = 5.68$* (Yates' correction).

* Significant at between the one per cent and two per cent levels of confidence.

Discussion

The need for a broader base and greater usefulness of our clinical understanding cannot be sufficiently stressed. Useful as the psychodiagnosis of the schizophrenic disorder is, it is not enough if we hope to be able to appraise the total functioning organism. One of the primary problems that confronts us in the appraisal of the schizophrenic disorder is the extent of physiological imbalance which accompanies an existing or incipient schizophrenic withdrawal. It is felt that this study emphasizes the importance that one must assign to the influence of the autonomic nervous system in the etiology and prognosis of schizophrenia. While this investigation did not deal with etiological considerations, it was concerned with the prognostic implications that a knowledge of autonomic nervous system sensitivity would entail. Further research will have to determine whether autonomic nervous system imbalance can be viewed as a causative, a concomitant, or a predisposing agent in the development of schizophrenia. It may not be unlikely that all three possible influences of the autonomic nervous system must be considered in the evaluation of the individual case.

The motivation that led to the present investigation had been to inquire into the prognostic significance of the Funkenstein autonomic nervous system test (11) as related to behavioral adjustment, change, and outcome of untreated schizophrenic patients. Funkenstein (11) had been able to predict whether a patient would or would not recover from schizophrenia when treated with ECT or ICT. He had been able to distinguish between patients who recover from ECT and patients who recover from ICT, on the basis of characteristically different blood pressure reactions as a function of the injection of adrenergic and cholinergic drugs. What is so particularly remarkable about this finding is that no adequate theory has been offered to explain the curative aspects of either ECT or ICT. Furthermore it must be noted that no actual theoretical formulation has been offered to explain these characteristically different blood pressure reactions. It is a case in point in which empirical application is ahead of any satisfactory theoretical body of knowledge. Autonomic nervous system activity is still very much of a puzzle, a fact which the literature reflects (18).

This author has been much concerned with the empirical application of shock treatments to schizophrenic patients. We find here another example of empirical application without theoretical support. One of the most frequent questions arising in a state hospital setting is "Should one attempt shock treatment?" The answer to such a question, while peripherally involving such considerations as suicidal risk, uncontrollable violence, or age factor, requires largely an intuitive affirmation or rejection. Extent of custodial care available and the dynamics of the personality of the physician will often be the crucial factors in such a decision. It is quite readily apparent that such shock methods as ECT, ICT, camphor injections, ammonia injections, metrazol and triazol injections, acetylcholine shock, pure nitrogen inhalation, and extended sedation therapy, all constitute severe trauma to the organism. It is unknown to what extent different organisms will differ in their reaction sensitivity to such treatments. It is not even known to what extent organisms will react in a like manner to such shock treatments as a function of the shock proper (18). If one were able to predict more accurately which patients would improve spontaneously without intervening shock treatment, such a hit-and-miss application would be reduced to patients who react unfavorably to the procedure used in this investigation. While Funkenstein's autonomic nervous system test (11) has been successful in predicting success or failure of shock treatment, it appeared to be highly desirable to utilize this test in an effort to investigate the course of illness without shock treatment.

Results of the study support the considerable prognostic significance of a patient's reaction sensitivity to the cholinergic drug, mecholyl chloride. Favorable blood pressure reaction, indicated by a blood pressure fall, was related significantly to spontaneous improvement. It was shown furthermore that 5 months after the initial experiment a significantly larger number of patients, who had responded favorably to the cholinergic drug injection, had been discharged from the hospital. Practical application of this finding appears self-evident. The actual time consumed in administering the test takes approximately one-half hour. The test can be administered by a nurse without direct medical supervision. Results of the test can easily be entered routinely into the patient's medical chart. It is a measure that will help the physician in his decision whether or not to attempt shock treatment.

This investigation could not establish any dependable relationship between reaction to the adrenergic drug epinephrine and behavioral adjustment. Funkenstein's findings have likewise been less conclusive in this respect (11). He stresses the important element of subjectively experienced anxiety reported by schizophrenic patients when subjected to epinephrine injections. In cases of extremely large blood pressure increase after epinephrine injection, prognosis following shock treatment was reported as poor (11). This investigator saw no adequate way to measure the subjective elements of the patient's reaction to epinephrine. In only three subjects out of the total group of 60 did the patient express verbally a feeling of dread. Nevertheless, a routine injection of epinephrine to newly admitted schizophrenic patients may be valuable as a further help in predicting reaction to shock treatment, provided anxiety is evidenced. Lack of such anxiety, however, cannot be assumed to counter indicate spontaneous improvement.

Summary

Findings with regard to the cholinergic drug mecholyl chloride supported the three major hypotheses. A significant relationship was established between increase of blood pressure following mecholyl chloride injection and poor behavioral adjustment, with an r of −.527. A significant relationship between decrease of blood pressure following mecholyl chloride injection and good behavioral adjustment was established, with an r of .425. Using t tests, mean differences were determined between first and eighth week behavior ratings for those subjects with the 15 highest and 15 lowest blood pressure reactions to mecholyl chloride. A t of 3.068, significant at the less than one per cent level of confidence in the direction of behavioral decrement, was obtained for the 15 highest blood pressure increases. A t of 1.818, significant at the less than five per cent level of confidence in the direction of behavioral improvement, was obtained for the 15 largest blood pressure decreases. Behavior ratings were significantly different for the first week and eighth week of behavioral observation for the 15 largest blood pressure increases and decreases. These differences were in the expected direction.

A follow-up study, 5 months after the initial experiment, revealed that out of the original group of 60 patients, 32 had been discharged on parole, 19 were institutionalized while nine were of indeterminate status and were not included. The relationship between hospital status and blood pressure reaction after the injection of mecholyl chloride was investigated by a Chi square analysis. A Chi square of 5.68 was obtained and found to be significant at the .01–.02 levels of confidence. Prolonged institutionalization is related to an abnormal blood pressure reaction after the injection of mecholyl chloride, while a normal reaction tends to be associated with early hospital discharge.

It has been demonstrated that reaction sensitivity of the autonomic nervous system, as indicated by blood pressure changes after the injection of a cholinergic drug, is a valuable tool in the prediction of behavioral adjustment and spontaneous behavioral changes. It also helps in predicting the status of patients with regard to prolonged hospitalization versus early hospital discharge.

BIBLIOGRAPHY

1. Angyal, A., and Blackman, N.: Vestibular reactivity in schizophrenia. *Arch. Neurol. & Psychiat., 44:* 611–620, 1940.
2. Angyal, A., Freeman, H., and Hoskins, R. G.: Physiologic aspects of schizophrenic withdrawal. *Arch. Neurol. & Psychiat., 44:* 621–626, 1940.
3. Bellak, L.: *Dementia Praecox.* The past decade's work and present status. A review and evaluation. New York: Grune & Stratton, 1948.
4. Bleuler, E.: *Dementia Praecox, or the Group of Schizophrenias.* New York: International Universities Press, 1950.
5. Cannon, W. B.: *The Wisdom of the Body.* New York: W. W. Norton, 1932.
6. Cohen, L. H., and Fiernan, J.: Metabolic, cardiovascular, and bio-chemical changes associated with experimentally induced hyperthyroidism in schizophrenia. *Endocrinology, 22:* 548–558, 1938.
7. Ficca, S. C.: The relationship of autonomic blood pressure types and subjects' performance on the Wechsler-Bellevue and Rorschach test. Unpublished Ph.D. Thesis, Pennsylvania State University, 1950.
8. Freeman, G. L., and Katzoff, E. T.: Individual differences in physiological reactions to stimulation and their relations to other measures of emotionality. *J. Exper. Psychol., 31:* 527–537, 1942.
9. Freeman, G. L., and Pathman, J. H.: Physiological reactions of psychotics to experimentally induced displacement. *Am. J. Psychiat., 100:* 406–412, 1943–1944.
10. Freeman, H., and Carmichael, H. T.: A pharmacodynamic investigation of the autonomic nervous system in schizophrenia. *Arch. Neurol. & Psychiat., 33:* 342–352, 1935.
11. Funkenstein, D. H.: Autonomic nervous system changes following electric shock therapy. *J. Nerv. & Ment. Dis., 108:* 409–422, 1948.
12. Funkenstein, D. H., Greenblatt, M., Root, S., and Solomon, H. C.: Psycho-physiological study of mentally ill patients. Changes in the reactions to Epinephrine and Mecholyl Chloride after electric shock treatment. *Am. J. Psychiat., 106:* 116–121, 1949–1950.
13. Funkenstein, D. H., Greenblatt, M., and Solomon, H. C.: An autonomic nervous system test of prognostic significance in relation to electroshock treatment. *Psychosom. Med., 14:* 347–362, 1952.
14. Funkenstein, D. H., Greenblatt, M., and Solomon, H. C.: Autonomic changes paralleling psychologic changes in mentally ill patients. *J. Nerv. & Ment. Dis., 114:* 1–18, 1951.
15. Goodman, L. S., and Gilman, A.: *The Pharmacological Basis of Therapeutics.* A textbook of pharmacology, toxicology and therapeutics for physicians and medical students. New York: The Macmillan Company, 1941.
16. Hoagland, H.: *Metabolic and Physiologic Disturbances in the Psychoses.* In 27th annual conference of the Hilbank Memorial Fund. New York: Harper, 1950.
17. Hoskins, R. G.: Oxygen metabolism in schizophrenia. *Arch. Neurol. & Psychiat., 38:* 1261–1270, 1937.

18. Hoskins, R. G.: *The Biology of Schizophrenia.* New York: W. H. Norton & Co., 1946.
19. Kantor, R: E., Wallner, J. H., and Winder, G. L.: Process and reactive schizophrenia. *J. Consult. Psychol., 17:* 157–162, 1953.
20. LeVay, D.: Hans Selye and a unitary concept of disease. *Brit. J. Sc., 3:* 157–168, 1952.
21. Meadow, A.: Anxiety, concrete thinking, and blood pressure changes in schizophrenia. Unpublished Ph.D. Thesis, Harvard University, 1950.
22. Meadow, A., and Funkenstein, D. H.: The relationship of abstract thinking to the autonomic nervous system in schizophrenia. In Hoch, P., and Zubin, J. (Eds.) *Relation of Psychological Tests to Psychiatry.* New York: Grune & Stratton, 1952.
23. Meadow, A., Greenblatt, M., Funkenstein, D. H., and Solomon, H. C.: Relationship between capacity for abstraction in schizophrenia and physiological response to autonomic drugs. *J. Nerv. & Ment. Dis., 118:* 332–338, 1953.
24. Pincus, G., and Hoagland, H.: Adrenal cortical responses to stress in normal men and in those with personality disorders. *Am. J. Psychiat., 106:* 641–650, 1949–1950.
25. Pincus, G., Hoagland, H., Freeman, H., Elmadjian, F., and Romanoff, L. P.: A study of pituitary-adrenocortical function in normal and psychotic man. *Psychosom. Med., 11:* 74–101, 1949.
26. Rubin, M. A.: Effect of hyperventilation on electro-encephalogram of schizophrenic subjects. *Arch. Neurol. & Psychiat., 48:* 968–976, 1942.
27. Schrader, P. J., and Robinson, M. F.: An evaluation of pre-frontal lobotomy through ward behavior observation with the Gardner Behavior Charts. *J. Abnorm. Soc. Psychol., 40:* 61–69, 1945.
28. Selye, H.: The general adaptation syndrome and the diseases of adaptation. *J. Clin. Endocrin., 6:* 117–230, 1946.
29. Wilcox, P. H.: The Gardner Behavior Chart. *Am. J. Psychiat., 98:* 874–880, 1942.

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DREAM RECALL AND EYE MOVEMENTS DURING SLEEP IN SCHIZOPHRENICS AND NORMALS

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Aserinsky and Kleitman (2) have recently reported the occurrence of rapid, jerky, conjugate eye movements during sleep and an association of these movements with dreaming. They studied 26 subjects and observed discrete periods of eye motility in all but four. Ten subjects were awakened 27 times while the eye movements were present, and in 20 instances were able to recall with great clarity the content of their dreams. In 23 awakenings during ocular quiescence, there were only two instances of dream recall.

The following study of schizophrenics and normals was undertaken, under the stimulus of these observations, with three aims: 1) to gather confirmatory data relating dream recall to eye movements; 2) to see if schizophrenics exhibited rapid eye movements during sleep; and 3) if so, to utilize the possible association with dreaming to gather data on psychotic dream content.

METHOD OF STUDY

The subjects were 17 chronic schizophrenics, nine males and eight females, ranging in age from 21 to 53, and a normal group of 13 medical students, all males, aged 22 to 32. All were presumably in good physical health. The schizophrenics were picked randomly from a larger group being studied at the Manteno State Hospital (1), stipulating only that they be manageable and at least to a slight degree communicative. Two schizophrenic females had undergone bilateral prefrontal lobotomies approximately 2 months prior to being used as subjects, and two schizophrenic males were studied both before and after a course of convulsive therapy (10).

Continual recordings of eye movements and brain waves were made on two subjects at a time during an average night's sleep without sedation. Supra-orbital, infra-orbital, parietal, and ear electrodes were affixed to each subject and the potentials led into a Grass eight-channel electroencephalograph in an adjoining room. Four pens were allotted to each subject. One pen recorded parietal brain waves, one, eye movements bipolarly from the supra-orbital lead referred to the infra-orbital, and the other two, eye movements monopolarly from the two orbital leads referred to the ears. Changes in the corneo-retinal potential field, as the eyeball rotated, were probably responsible for the electrical impulses generated (5). Eye movement potentials were out of phase on the two monopolar pens, while large brain waves were in phase. Furthermore, eye movement potentials were larger on the bipolar pen, and the spread from high voltage brain waves showed up larger on the two monopolar pens. Thus, there was a double differentiation between eye movement potentials and EEG artifacts. Vertical movements gave the largest potentials in this method of recording, with movements in other directions varying approximately as the cosine of the angle of displacement from the vertical. Horizontal movements showed little or no potential. However, preliminary studies indicated that periods of ocular motility contained movements in all directions, and since the aim was to establish only the presence or absence of movements, not to analyze or quantify them, this method was felt to be satisfactory.

The subjects were instructed to go to sleep in their usual fashion, the lights were turned off, and from this point on at least 1 minute of record was taken every 5 minutes throughout the night. A fair amount of waking record was obtained before the onset of sleep in most cases. All the subjects had good waking eye movement potentials and, with one exception, were alpha dominant or mixed alpha brain wave types (insofar as this rhythm appeared in the parietal leads). The electrical recordings of the eye movements were occasionally confirmed by direct observation.

The onset of sleep was arbitrarily defined as the time of appearance of the first sleep spindles in the brain wave record. In most cases, this occurred very shortly after the disappearance of alpha rhythm, with only a short interval of the so-called "drifting" or "drowsy" EEG. Criteria of spontaneous awakening during the night were a reappearance of alpha rhythm, excessive body movement, opening the eyes, and calling out to the experimenter. The schizophrenics averaged about 7 hours of sleep per night and the medical students about 6.

On certain nights, mixed irregularly among the others, subjects were awakened during eye movement periods and asked whether they were dreaming and, if so, to relate the content of the dream. A control series of awakenings was done during periods when there were no eye movements, and the EEG was roughly similar to that seen during eye movement periods. In all cases, the questions and awakening procedures were identical. The subjects, of course, were not told whether their eyes had been moving.

Before the experiments began, the subjects were questioned about their dream activity. None admitted dreaming more frequently than once or twice a month, and four of the schizophrenics stated that they never dreamt. The schizophrenic subjects were questioned daily about the previous night's dream activity for 6 days prior to being observed during sleep. This was to accustom them to being interrogated and to see if the process of questioning produced any change in their ability to recall dream material.

With few exceptions the subjects had little difficulty in falling asleep. The schizophrenics accepted the experimental situation quite calmly. In only one or two instances did they show evidence of fright, and these were on first nights in the new situation.

The chronic schizophrenics accounted for a total of 55 nights, with a range of 1 to 7 nights per subject, while the medical students slept 30 nights, 1 to 9 nights per subject.

RESULTS

Eye motility. One normal subject who was observed only a single night failed to show rapid eye movements during sleep. Three schizophrenics and one medical student did not exhibit eye movements on the first night but showed them on subsequent nights. Rapid eye movements were seen in all others every night they slept.

The eye movements occurred in discrete periods, but the eyes were not constantly in motion during such a period. Rather, the activity occurred in irregular bursts of one or two movements—up to 20 or 30. The bursts were usually separated by a few seconds of quiescence although occasionally 4 or 5 minutes passed without a movement. A period of eye motility was thus delimited by periods of quiescence on either side, lasting more than 5 minutes, and almost always these quiescent periods were of the order of 40 to 60 minutes. A single movement generally took place in 0.2 seconds and was followed by a fixational pause of varying duration. There was no pattern to the direction of the movements. Occasionally, on direct observation, several small jerks in one direction were seen, or there were bursts of movements through large arcs in all directions. As many as six movements were counted in a period of 2 seconds although the number was usually less. The amount of activity varied widely from period to period and from night to night. No relationship of the amount of movement to the time of the period or to a particular subject could be demonstrated, nor was there any apparent relation to age or sex. The movements were easily seen on direct observation with a very dim light, in spite of the closed eyelids. This was documented by Aserinsky and Kleitman who were able to take motion pictures of the eye movements in two subjects. The subjective impression was that the eye movements resembled those of an individual scanning his environment or watching some event associated with a great deal of movement and activity.

In general, a night's record for any single individual showed a periodic occurrence of eye movements, alternating with ocular quiescence The periods averaged approximately 20 minutes in length and tended to be longer the later in the night they appeared. Those occurring about an hour after the onset of sleep were usually around 5 minutes in length, while those near the end of the night often lasted for more than 30 minutes. The chronic schizophrenics averaged one rapid eye movement period every 1.60 hours, while for the normals the ratio was 1.55. Waking the subjects seemed to have almost no effect on the

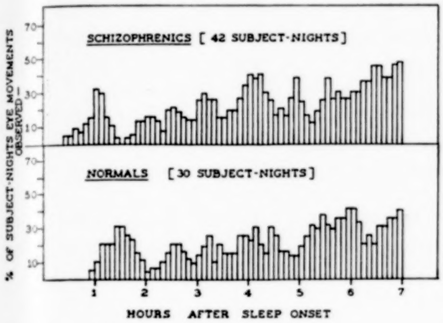

FIG. 1. Incidence of eye movements in successive six-minute periods after the onset of sleep.

over-all pattern except in rare instances when the subjects remained awake. In 118 awakenings during eye movement periods, there were 25 instances of recurrence immediately on falling asleep again. Whether the remaining 93 were artificially shortened or were about to end by themselves cannot be said. Eye movements never occurred immediately on returning to sleep from the control awakenings. In addition, there were only two instances of eye movements immediately after the initial onset of sleep, both occurring in the same subject after about 3 hours of tossing and turning. There was a considerable variation in the pattern of occurrence of periods of eye motility from subject to subject and from night to night, but an over-all regularity was maintained.

The graphs in figure 1 show a summation of the eye movement periods for the two groups of subjects. The vertical bars indicate the percentage of subjects showing eye movements at any time during successive 6-minute periods after the onset of sleep. Infrequent large periods of wakefulness have been deleted, and the sleep considered continuous. As can be seen, the records of the two groups, schizophrenics and normals, are roughly similar. Periodicity is not easily compared. In the graphs, both groups have an early peak of eye movement activity at about 1 hour after the onset of sleep, followed by subsequent peaks. However, as time progresses, individual differences tend to have a cancelling effect and flatten the histograms. The initial peak in the schizophrenics seemed to occur somewhat earlier than in the medical students. However, the difference of the means of the time of onset of the eye movement periods making up the initial peaks in the two groups was not significant. It must be remembered that figure 1 does not give an absolutely exact picture of the quantity of eye movement as many periods were terminated by interrogations.

The data obtained on the two females with bilateral prefrontal lobotomies and the two males after convulsive therapy were at least qualitatively similar to those obtained from the other subjects. In addition, no change in eye motility was noted in the two male psychotics, with reference to data obtained before convulsive therapy, although the EEG showed marked slowing.

Association of dream recall and eye movements. There was no apparent change in the schizophrenics' ability to recall dreams during the 6-day period of questioning prior to being studied during sleep. Among all 17, only three recalled a single dream.

Twelve schizophrenic subjects in 24 nights were awakened 95 times, 67 during eye movement periods and 28 during periods of ocular quiescence. Ten normals were awakened 70 times in 18 nights, 51 during eye movement periods and 19 during control periods. The replies to interrogation fell into four categories: the subjects (a) remembered dreaming and were able to recall the content quite vividly; (b) remembered dreaming but were unable to recall any of the content, or at best, quite

TABLE 1.—RESULTS OF INTERROGATION DURING PERIODS OF EYE MOVEMENT AND PERIODS OF OCULAR QUIESCENCE

	Eye Movement				Quiescence			
	Positive		Negative		Positive		Negative	
	Subject recalls dream vividly	Subject remembers dreaming but cannot recall content	Subject uncertain whether or not was dreaming	Subject certain was not dreaming	Subject recalls dream vividly	Subject remembers dreaming but cannot recall content	Subject uncertain whether or not was dreaming	Subject certain was not dreaming
Schizophrenics...	40	12	5	10	0	3	2	23
Normals.....	45	2	3	1	0	0	4	15

vaguely; (c) were unsure whether or not they had been dreaming; (d) felt sure that they had not been dreaming. The first two categories were considered positive and the last two negative. From table 1 it can be seen that the schizophrenics gave 79 per cent positive replies and 60 per cent dream recall when awakened during eye movements, while the normals gave 92 per cent positive replies and 88 per cent dream recall. The over-all total for both groups was 72 per cent dream recall after eye movement interrogation, as opposed to 0 after control awakenings. Every subject in the two groups gave at least one positive reply to the eye movement interrogations.

TABLE 2.—EXAMPLES OF SCHIZOPHRENIC DREAMS

1. Q.—Were you dreaming?
   A.—Yes.
   Q.—What about?
   A.—A hat.
   Q.—Is that all?
   A.—Yes.
   Q.—Just a hat?
   A.—Yes.
   Q.—Were you wearing it?
   A.—No.

2. Q.—Were you dreaming?
   A.—Yes.
   Q.—What about?
   A.—There was ah- ah- a trunk and curtain rods.
   Q.—A trunk and curtain rods?
   A.—Yes.
   Q.—What else?
   A.—Nothing.
   Q.—You mean there was nothing but just a trunk and curtain rods? No people?
   A.—Yes.
   Q.—Were you in it?
   A.—I don't think so. I saw them.

3. Q.—Were you dreaming?
   A.—Yes.
   Q.—What about?
   A.—A coat that was ripped.
   Q.—A coat that was ripped, is that all?
   A.—Yes. There's nothing in my dreams.

4. Q.—Were you dreaming?
   A.—Yes.
   Q.—What about?
   A.—A shelf.
   Q.—Is that all?
   A.—Yes.
   Q.—Just a shelf hanging in space?
   A.—Yes.

5. Q.—Were you dreaming?
   A.—Yes sure.
   Q.—What about?
   A.—A suitcase.
   Q.—Were you in the dream yourself?
   A.—No.
   Q.—Just a suitcase?
   A.—Yes.
   Q.—Was it doing anything?
   A.—No sir. It was just sitting there.

Dream content. It was assumed that the dream reports given immediately after awakening during a dream, if that is what actually occurred, would be much more reliable than those obtained by questioning subjects the next morning. It was hoped that this method might lead to the discovery of consistent and easily recognizable differences between schizophrenic and normal dream content. However, the only obvious difference was that about half of the chronic schizophrenics frequently reported dreams of isolated, inanimate objects, apparently hanging in space, with no overt action whatsoever. The control group of medical students did not report a single dream of this type. That these peculiar dream reports were probably not just the result of a deteriorated ability to communicate was brought out by the fact that the same patients described other dreams which seemed quite normal and were also able to communicate fairly adequately in the waking state. Several examples of these dream reports are given in table 2.

Electroencephalography. The purpose of recording the EEG was merely to obtain a check on whether subjects were asleep. It was felt that a single lead could serve this purpose well enough, and thus the EEG data are not very extensive. No abnormalities, either awake or asleep, were seen in the two groups except for the two lobotomized schizophrenics and the two post-convulsive schizophrenics, in whom slow waves were evident from the parietal region while awake. Figure 2 is a sample recording. Subject F. S. shows eye movement potentials. The out-of-phase relationship of the two monopolarly eye pens can be seen as well as the increased amplitude on the bipolarly pen. The other subject is in a period of ocular quiescence. The EEG during ocular quiescence was generally characterized by high voltage, low frequency waves early in the night with some spindling, and later by frequent well-defined spindles against a low voltage

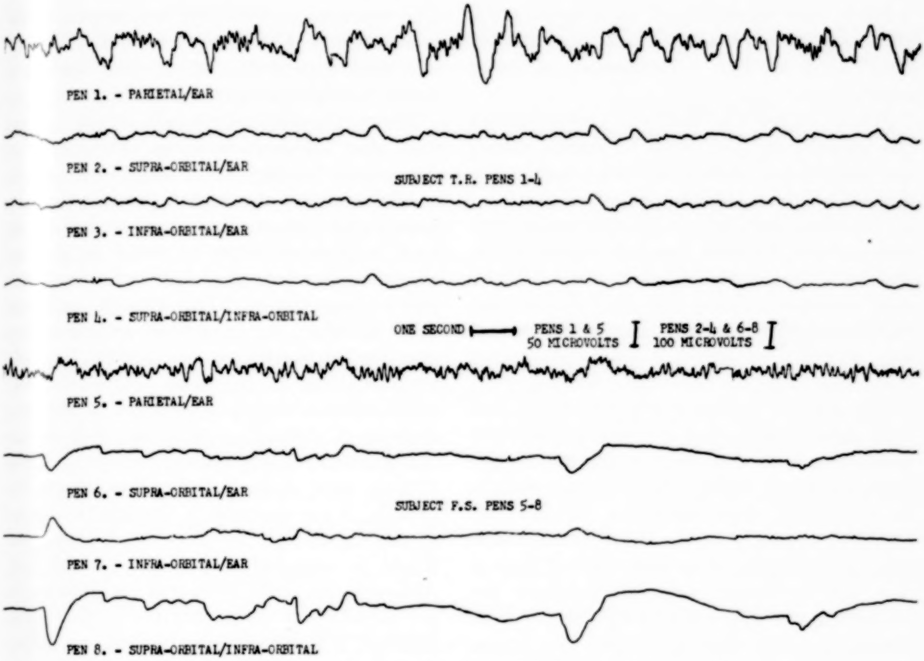

FIG. 2. Sample recording of eye motility and brain waves in two subjects.

background. During eye movement periods, spindles were not seen. Most waves fell into frequency ranges of 4–7 per sec. and 15–25 per sec. and were 50 microvolts or less.

DISCUSSION

It seems likely that chronic schizophrenics and normals have no marked inter-group differences with regard to the frequency and periodicity of rapid eye movements during sleep, nor in the quality of these movements.

In their original paper on rapid eye movements during sleep in normal subjects, Aserinsky and Kleitman indicated that the first eye movement periods occurred from 1 hour and 40 minutes to 4 hours and 50 minutes (3 hours and 14 minutes, mean) after the onset of sleep. In this study, it was found that in many instances the first periods occurred much earlier than this, from 40 to 90 minutes after the onset of sleep. Later work (4) with continuous recording, rather than sampling, has confirmed this. In the great majority of nights, an eye movement period occurred around 1 hour after the onset of sleep, and even when eye movements were not seen, there was at least a "lightening" of the brain waves.

The nights on which rapid eye movements were not seen were always first nights with any one subject. Thus, there appeared to be a tendency for eye movements to be suppressed on the first night that a subject slept in new surroundings. This is contrary to what one might expect if eye movements are in some way related to disturbed or restless sleep. On the other hand, if eye movements are part of a definite and contingent sleep pattern or rhythm, a restless or disturbed sleep should tend to disrupt their occurrence.

Aserinsky and Kleitman found 74% dream recall when awakened during eye movement periods which corresponds nicely to the overall figure of 72% for both groups in this study. The difference between the figure of 60% for the schizophrenics and 88% for the medical students seems best explained on the basis of the mental illness. Certain of the schizophrenics consistently replied negatively to interrogation regardless of whether awakened during eye motility or quiescence. The replies of these subjects were characterized by a monotonous stereotypy which made it doubtful that they represented a true verbalization of inner experiences.

If it is assumed that the dream visualizations the subjects recalled when awakened during eye movement periods actually took place during these periods, it appears that dreaming occurs much more frequently than was heretofore realized. In most previous studies of frequency of dreaming (9), even when subjects were awakened during the night rather than questioned the next day, it was the rare person who remembered dreaming more than once a night, and many did not recall dreaming at all. Subjects in the present study who stated that they dreamt only once or twice a year often recalled four or five lengthy dreams a night when awakened during eye movement periods. It is unlikely that there was simply more frequent dreaming in the experimental situation, as on nights when they showed four or five eye movement periods but were not awakened, the subjects usually did not recall dreaming. The objection that this dream recall was in response to the awakening stimulus is, of course, answered by the fact that no dream recall was elicited after the control awakenings.

On the basis of interview techniques, Boss (3), Kant (7) and Noble (8) have concluded that many schizophrenics dream as much as normals, but that some do not. Since no clear-cut instance of lack of rapid eye movements during sleep was found in any of the schizophrenics in this study, and the frequency of eye movement episodes in the schizophrenics and normals was virtually equal, it seems reasonable to conclude that schizophrenics dream as much as normals, including even those who persistently deny dreaming.

The dreams reported here were always approximately the same length whether the subject was awakened after 5 or after 50 minutes of eye movements. This probably means that only the dream material occurring just before awakening was remembered and that the remainder, presumably a large amount, was not recalled. It seems possible that each burst of eye motility, occurring in a single period, represented a dream episode. The appearance of the eye movements themselves suggested that they were a direct result of visual experience, rather than merely a result of heightened nervous activity.

The results of this study indicate that a great deal more information about the content of dreams can be obtained if subjects are awakened during eye movement periods, than by questioning them at other times, or even during such heightened states of recall as psychoanalytic therapy (6). But whether such information would have enough practical value to offset the trouble of getting it is a question for psychiatrists to answer. It would be premature, on the basis of the relatively small amount of dream material, to say that dreams of isolated, inanimate objects are characteristic of schizophrenic subjects. These dreams were elicited during eye movement periods. If eye movements are directly related to the visual content, little or no movement would be expected in a dream of this sort. Although this could mean that eye movements are not directly representative of the visual activity, it is more likely that the verbalizations represent a distorted schizophrenic concept of a more active visual experience. The fact that Boss, Kant, and Noble found no such dreams in the material of their schizophrenics from daytime questioning suggests the importance of nocturnal awakenings.

It is interesting to note that there were 25 instances of recurrence of rapid eye movements immediately on returning to sleep from eye movement awakenings. Seemingly, the period of heightened CNS activity had not run its course, and although the subjects were able to fall asleep, they continued to dream. On the other hand, when an awakening occurred during ocular quiescence, the return to sleep was never associated with an eye movement period. Nor was the time of onset of the next period markedly changed from what would have been expected in the absence of an awakening. Thus, the periods were neither initiated nor always ended by the disturbances. It seems likely, therefore, that the rapid eye movement periods and probably associated dream activities do not occur in response to random environmental stimuli, but are part of an intrinsic physiological sleep pattern.

SUMMARY

Periods of rapid eye movements were seen to occur during sleep in both schizophrenic and normal subjects. The quality of the movements, their pattern of occurrence, and the duration of the periods were virtually the same in the two groups. The initial period after the onset of sleep was observed to occur earlier in both groups than was previously reported in normals.

There was a high degree of association of dream recall and rapid eye movements in both groups confirming the report of Aserinsky and Kleitman. The suggestion was made that the discrete bursts of motility seen in a single period might represent single dream episodes and that the eye movements themselves might be a direct manifestation of the visual imagery.

A great deal of information about the content of their dreams was obtained from the subjects during the course of the study, and the schizophrenics differed from the non-schizophrenics in reporting many dreams of isolated, inanimate objects apparently hanging in space with no movement.

Thanks are extended to Dr. Nathaniel Apter for helpful criticism and for the use of patients under his supervision, to Dr. Paul Alfred Bay for the use of facilities and EEG equipment at the Manteno State Hospital and to Prof. Nathaniel Kleitman, for counsel during the experiments.

BIBLIOGRAPHY

1. Apter, N.: Research approaches to chronic schizophrenic reactions: Methodological problems. *Bull. Menninger Clin., 18:* 154, 1954.
2. Aserinsky, E., and Kleitman, N.: Regularly occurring periods of eye motility, and concomitant phenomena, during sleep. *Science, 118:* 273, 1953.
3. Boss, M.: Psychopathologie des Traumes. *Ztschr. f. d. ges. Neurol. u. Psychiat., 162:* 459, 1938.
4. Dement, W., and Kleitman, N.: Incidence of eye motility during sleep in relation to varying EEG pattern. *Federation Proc., 14:* 216, 1955.
5. Fenn, W., and Hursh, J.: Movements of the eyes when the lids are closed. *Am. J. Physiol., 118:* 8, 1937.
6. Fisher, C.: Studies on the nature of suggestion. I. Experimental induction of dreams by direct suggestion. *J. Am. Psychoanal. Assoc., 1:* 222, 1953.
7. Kant, O.: Differential diagnosis of schizophrenia in the light of the concept of personality stratification. *Am. J. Psychiat., 97:* 335, 1940.
8. Noble, D.: A study of dreams in schizophrenia and allied states. *Am. J. Psychiat., 107:* 612, 1951.
9. Ramsey, G.: Studies of dreaming. *Psychol. Bull., 50:* 432, 1953.
10. Reilly, R. et al.: Convulsant effects of isoniazid. *J. A. M. A., 152:* 1317, 1953.

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THE RORSCHACH HUMAN MOVEMENT RESPONSE AND ROLE TAKING BEHAVIOR[1,2]

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It is generally accepted that the M responses reveal the basic attitudes a person has toward others in his environment. These attitudes disclosed by the M, however, are almost universally believed to reside in the unconscious or in imagination. Piotrowski (8) took the opposite view that the M content was not repressed even when the subject was not aware of it, and that it directly influenced social behavior. Nevertheless, little, if any, experimentation has been done to determine whether or not the M scores were correlated positively with overt social conduct. It is the purpose of this study to investigate, in a systematic fashion, whether the attitudes expressed in the Rorschach M responses are revealed in direct, overt behavior.

Rorschach (12), who was greatly influenced by Mourly Vold's (2) systematic research on the psychophysiology of dreams, postulated an inverse relationship between kinesthetic perceptions and physical activity. On the other hand, largely on the basis of his empirical observations and clinical acumen, he indicated the possibility of a direct correspondence between the M attitudes and overt behavior. Thus, he stated, "Subjects who interpret extention kinaesthesias are active individuals with strong drives towards importance and activity although they frequently show neurotic inhibitions. Those who see flexion kinaesthesias have passive and resigned natures" (12, p. 206). Oberholzer expressed it by saying, "The M series is, therefore, what is 'lived'. I purposely avoid saying 'experienced' in order not to imply that the patient knows the nature of this experience. M is the compulsion determining what is lived, and how it is lived . . ." (12, p. 208). The life meant here is the inner life, the fantasies, more exactly the unconscious tendencies which by definition are not manifested in overt behavior.

Piotrowski expressed the view that the attitude of the M response was reflected directly in overt behavior: "The M's represent the conception of life according to which the individual makes his adjustment to reality. The M stands for the most individual and integrated strivings which dominate the individual's life. Thus the M indicates traits stabilizing the relation between the individual and his environment" (8, p. 149). In his later writings, Piotrowski reformulated this view in a more precise manner by stating that "the M always reveals the subject's conception of role-in-life. The conception of role-in-life denotes a definite tendency, deeply embedded in the subject and not easily modified, to assume an unchanging attitude or attitudes when dealing with others recognized by the individual as vitally important to him. This does not mean that the subject is incapable of acting, even in vital matters, in a manner incompatible with his basic conception of role. However, it implies that acting inconsistently with one's conception of role causes anxiety and decreases the efficient handling of important life problems" (9, p. 560).

Recently, Phillips and Smith (7) have expressed a point of view which appears to be in agreement with that of Piotrowski. According to these authors, the M response reflects some aspect of role taking and role assigning. They wrote, "The clinical significance of the movement responses derives from the ultimate relationship between attitudes in the movement percept and habitual attitudes (hence role-playing and behavior in the extra-Rorschach situation). That is, in his movement responses the individual tends to perceive attitudes with which he characteristically empathizes" (7, p. 75).

Beck (1), Klopfer and Sender (3), and Schachtel (13), however, stand in opposition to the above-mentioned views. According to Beck, the M is never reflected directly in overt behavior; rather they are one's wish-fulfilling activities which dare not find expression.

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[1] This paper is a by-product of the author's doctoral dissertation.

[2] The author wishes to express his indebtedness to Drs. Z. Piotrowski and J. R. Wittenborn for their valuable aid and advice.

Similarly, Schachtel feels that the attitudes revealed by the M do not necessarily mean that they are expressed in a person's manifest behavior. "All that one can say is that the strivings expressed in kinesthetic percepts are dynamically important tendencies in the personality structure. They may be needs and strivings of which the subject is aware, but that does not mean that they guide his purposeful behavior" (13, p. 87). Schachtel goes on to state that the M response indicates some unsatisfied tension regarding the particular need and cites as his rationale the inverse relationship observed by Rorschach between kinesthetic perception and motor activity. Klopfer defines the meaning of the M in the following terms: "M indicates activity of inner life in the realm of imagination or intuition" (3, p. 20). "M is an indicator of inner stability . . . is also related to the capacity for self-realization . . . M can best be described as 'ego tolerance for archaic forces' " (4, p. 576). Nearly all writers on the M agree with Rorschach that the M reveals in Beck's words "mental activities in which we should like to engage in the outer world but cannot, or dare not" (1, p. 92).

On the basis of the evidence cited by Piotrowski and Schreiber (11) and the writer's clinical experience, it was felt that the role taking behavior suggested by the M response was reflected in extra-Rorschach behavior.

PROCEDURE

Subjects

The subjects comprised 30 chronic male schizophrenics hospitalized at a VA neuropsychiatric hospital. They were randomly selected from a group of cooperative patients in relatively good contact. It was felt that this was a feasible clinical group to employ because schizophrenics, more so than normals, express both their conscious and unconscious attitudes and behavior in a more direct fashion. In schizophrenics there is an absence of defenses whereas normals can more easily mask and obscure their real feelings and attitudes.

Methodology

Although the methodology has been reported in a previous paper (6) in connection with another study, it is felt that for the sake of clarity it is necessary to repeat some of the important details in this paper. An experimental interpersonal situation was created in which the subject was told a short story and instructed to relate it to the interlocutor. The interlocutor purposely created an argumentative situation by disagreeing with the subject's story; they both were required to discuss these differences and arrive at a mutually acceptable solution. The subjects were specifically instructed to discuss any differences which arose and to work with the interlocutor in an attempt to resolve these differences. Participants in the experiment, then, were the subject and an interlocutor (the writer). An experimenter (a third person), after having established rapport with the subject, introduced him to the experimental situation as follows:

"We are interested in knowing what happens when one person hears a story and another person sees it on pictures. I am going to tell you a story about a young man. Later, you are going to tell the story to another person, so listen carefully. He will have already seen the story on pictures. I have told him to stop you when his ideas differ from yours or if he wants to make a change in the story, and both of you will talk it over to see if you can agree. We know that sometimes people have differences of opinion; nevertheless both of you will try to work out the best version of the story between yourselves."

The subject was informed that the discussion would be recorded on a tape recorder.

The following story was told to the subject:

> Johnny was walking along the street one evening when suddenly it began to rain. In order to avoid getting wet he ran into a bar. He sat down at the bar and had a few drinks. Then he noticed a beautiful girl sitting alone in a booth. He walked over and started to talk to her. Then they had a few drinks together. He mentioned that his house wasn't too far away and asked her if she would like to come up for awhile. She refused and walked out of the bar. Johnny left the place right after her.

The subject was requested to recite the story until he was able to recall its major details. If necessary the experimenter repeated the story to a maximum of three repetitions. After the subject had mastered the main points of the story, he was taken to another room where he and the interlocutor (whose identity was not known to the subject) were introduced to each other. The experimenter then instructed the subject to tell the story to the interlocutor. He also gave the instruction that if there were any disagreements they were to be discussed with the view of reaching a compromise and working out one story between the two of them. The experimenter then left the room. Upon completion of the conversation he was recalled and asked the subject to relate the story that had been agreed upon.

The subject was generally given the Rorschach test before he participated in the experiment. His performance in the experimental situaton was compared with his M responses on the Rorschach.

Analysis of the data

Three independent judges scored the Rorschach M responses in terms of self-assertive M's, indecisive M's,[3] and compliant M's. A self-assertive M is one in which a person overcomes the force of gravity. A compliant M is one in which a person gives in to the force of gravity. An indecisive M is one in which a person overcomes and gives in to the force of gravity. Agreement between at least two out of three judges constituted acceptance of a score.

The writer judged the subject's performance in the experimental interpersonal situation in terms of his ability to cooperate in collaborating with the interlocutor in accomplishing the task. Here, the writer was guided by the analysis done in his previous study where the criteria for role taking behavior and relationship to the task were developed. The criteria which indicated that the subject's behavior remained unmodified despite interpersonal influences, and the criteria which reflected impaired task orientation were employed in this study to mirror self-assertive role taking. This type of behavior was manifested by the subject, for example, when he rigidly adhered to the details of his own story; when he ignored the interlocutor's statements and abandoned the discussion at hand; when he merely parroted back the remarks of the interlocutor or persistently interrupted him. In brief, the subject either refused or was unable to collaborate with the interlocutor in accomplishing the task. Rather, he appeared to be intent on demonstrating his independence and self-reliance.

The criteria which indicated the subject's behavior was genuinely modified by interpersonal relations were employed in this study to reflect compliant role taking. Here, the subject acted as though he was being guided by the interlocutor; he accepted the interlocutor's suggestions and story details and compromised with him in order to complete the task.

The quality of the subject's M responses on the Rorschach test and his performance in the interpersonal situation were compared and statistically analyzed by the use of Chi square.

Results

Table 1 presents 29 subjects classified simultaneously with respect to role taking behavior and the quality of the M response. It can be seen that eight subjects produced only self-assertive M's, and in all of these cases the type of role taking behavior was predominantly self-assertive. Twelve subjects did not produce any M responses. Eight of these subjects evidenced role taking behavior which was predominantly self-assertive; the remaining four were self-assertive in the beginning of the experimental situation but finally complied with the interlocutor in accomplishing the task. Nine of the subjects produced compliant M's, and in all of these cases their role taking behavior was predominantly compliant. An inspection of table 1, then, reveals a high correspondence between the quality of the M produced by the subject and his role taking behavior.

In order to provide a statistical test of the hypothesis that role taking behavior and the quality of the M are independent, table 2 was prepared: those subjects who gave only self-assertive M's are distinguished from all others regardless of M, and those subjects whose role taking was predominantly self-assertive are distinguished from all other patients. This combination of the data (provided by table 1) results in a fourfold contingency table which enables us to use Chi square with Yate's correction in testing the null hypothesis, i.e., the hypothesis of an

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[3] Indecisive M was discarded from the analysis because only one was given out of a total of 34 M responses.

TABLE 1.—Twenty-nine Subjects Classified Simultaneously with Respect to Role Taking Behavior and with Respect to the Quality of the M

Quality of M	Role Taking Behavior			
	Predominantly compliant role	Self-assertive to compliant role	Predominantly self-assertive role	Σ
Self-assertive only	0	0	8	8
No M	0	4	8	12
Self-assertive and/or compliant	9	0	0	9
Totals	9	4	16	29*

* One subject rejected the Rorschach test.

TABLE 2.—A Chi Square Test for Hypothesis That Role Taking Behavior is Independent of the Quality of the M

	Predominantly Compliant Role	Predominantly Self-Assertive Role	Σ
Subjects with only self-assertive M	0	8	8
Subjects with self-assertive and/or compliant M, and with no M	13	8	21
Totals	13	16	29

Chi square = 8.3 = P <.01 level of confidence.

independence and no relationship. As can be seen from table 2, the null hypothesis is rejected at the .01 level of confidence. Therefore, self-assertion in the M and self-assertion in role taking behavior appear to be significantly related to one another in that they reflect a common mode of response.

Discussion

The results of the study support the hypothesis that the quality of the M is reflected in social role taking behavior. The schizophrenics who gave only self-assertive M's rigidly adhered to the details of their own story and generally refused to cooperate with the interlocutor in order to reconcile the conflicting viewpoints. Their behavior remained, to a great extent, unmodified in the social situation. In being so unyielding and independent it appeared that they were attempting to fulfill their need for leaving an imprint of their personality on the interlocutor. Those schizophrenics who gave both self-assertive and compliant M's were, in the beginning, quite rigid and independent, but toward the end of the experimental situation they cooperated with the interlocutor in resolving some of the discrepancies between the two stories. In accepting some of the interlocutor's suggestions and in complying with the task instructions they demonstrated their need to lean on other people and be influenced by them. The majority of the schizophrenics who didn't give any M were self-assertive although some of them showed both self-assertive and compliant behavior. Their behavior during the experiment may have been a function of a number of other factors and not of (or aside from) their conceptions of life role.

The results of the study are all the more striking when one considers that chronic schizophrenics are very much inclined to be negativistic, resentful, and contrary. The fact that all patients with compliant M behaved in a compliant manner in the experimental situation is remarkable. That all patients with self-assertive M behaved in a self-assertive manner during the experiment also is remarkable in view of strong anxieties.

The question naturally arises as to whether the same results would be obtained if a normal population was employed. On theoretical grounds the writer's adherence to the principle of "genetic parallelism", as formulated by Werner (16), would prompt him to answer in the affirmative. The principle stresses the similarity as well as the difference of comparative developmental relationships. Furthermore, there is empirical evidence to suggest that these results would reliably be obtained from normals. Piotrowski (8), for example, cites the record of a normal married woman who, because of adverse experiences, resigned herself to a life different from that of her happy childhood. Her Rorschach contained the following M response: "Two gentlemen bowing low in an affected manner". Certainly, more definitive studies with normal subjects are needed.

In this study the quality of role taking behavior was described in terms of self-assertion, indecision, and compliance. The writer is aware that a variety of attitudes may be expressed both in overt behavior and in the

M response. However, the patterns of attitudes which interact to form an individual's social role were focused upon. Basically, the patterns of habitual attitudes and responses may be conceived of as falling along the self-assertion-compliance continuum. It is this dimension of role taking behavior that is of critical importance.

It is the opinion of this writer that the tendencies indicated by the M response continually strive for direct, overt expression. These tendencies appear to be deep, basic strivings to relate to others in a certain typical manner, tendencies which are almost always manifested in situations which the individual considers to be extremely important to him. An acute emotional disturbance, however, may delay or suppress this tendency. In order to predict from a Rorschach protocol whether or not an individual's role will be evidenced in overt behavior, it is likely that prediction will be improved by considering other test indices such as the M: sum C, W:M, the shading responses, etc. (9, p. 567) In this writer's opinion, M is the most influential of all of the determinants and other test factors and thus of primary significance in predicting behavior. Singer and Spohn have restated this when they wrote, ". . . it seems clear that as a perceptual or apperceptual phenomenon presumably exemplifying some general behavioral principle, the human movement response to the Rorschach inkblots has definite correlates in behavior quite apart from the immediate testing situation" (15, p. 7).

The viewpoint of Beck (1) and Schachtel (13) is in opposition to the one taken in this paper. Beck, for example, feels that since M represents one's unfulfilled wishes, it is never expressed in overt behavior. Both of the above-mentioned investigators base their conclusion on Rorschach's assumption that there is an inverse relationship between the perception of kinesthesia and motor activity. And recently a number of experiments have been reported in the literature which, on the surface, appear to support this assumption (5, 14).

The experiments which were carried out to substantiate Rorschach's claim that there is a negative correlation between the number of M's and amount of overt motor behavior were concerned with the problem of whether interferences with free motor behavior would facilitate the production of M. The experimental results supported this theoretical point. But this problem is not the object of this investigation. Piotrowski (10) directed attention to the fundamental difference between the two problems related to the M. One problem is that which is stated above, viz., whether there is an inverse relationship between the "perception" of the M and the amount of motor activity. The other problem is whether the conceptions of role-in-life revealed in the content of the M actually and directly influence the handling of others in personally vital social interactions, or whether these conceptions reflect repressed and unfulfilled imaginary tendencies. These are two different problems. Available evidence shows that the production of the M is facilitated by the restraint of motor activity to some limited extent. This is a matter of the subject's communicating his M to the examiner. Clinical evidence was adduced to contribute to the support of the view that the M attitudes were reflected in overt motor behavior when personally vital matters were involved (11). The present investigation is the first attempt to test this view in an experimental setting.

Rorschach inferred from the negative correlation between amount of overt motor activity and number of M's that the M attitudes would not be reflected in overt social and motor behavior and that the greater the number of M's the greater would be the suppression of attitudes from acting out. This seems to be an unwarranted inference. There are several essential differences between the relation of the manifest dream content to overt activity, on the one hand, and the relation of the M content to overt activity, on the other (11). Laws applicable to one relation are not valid when applied to the other relation despite some similarities between them.

The writer is of the opinion that the attitudes or action tendencies disclosed by the M are generally manifested in social behavior. This is the main conclusion of the present investigation.

SUMMARY AND CONCLUSIONS

The purpose of the study was to investigate the relationship between the Rorschach human movement response and role taking behavior. The hypothesis advanced was that the nature of the M is reflected directly in social behavior.

The quality of the M's of 30 hospitalized chronic schizophrenics was compared to their role taking behavior in an experimental interpersonal situation. In this relatively structured situation the subject was told a short story and instructed to relate it to the interlocutor. The interlocutor, controlling the situation, purposely created an argumentative situation by disagreeing with the subject's story; the subject was required to discuss these differences and arrive at an acceptable solution.

Three judges independently scored the M responses in terms of self-assertive M's, indecisive M's, and compliant M's. A self-assertive M is one in which a person overcomes the force of gravity, e.g., "walking". A compliant M is one in which a person gives in to the force of gravity, e.g., "bending". An indecisive M is one in which a person overcomes and gives in to the force of gravity, e.g., "pushing and pulling". The subject's performance was rated in terms of his ability to cooperate in collaborating with the interlocutor in order to accomplish the task. His performance in the experimental situation was compared with his M scores on the Rorschach and statistically analyzed by the use of Chi square.

The results supported the experimental hypothesis. The schizophrenics who gave only self-assertive M's were unable to cooperate with the interlocutor in order to reconcile the discrepancies between the two stories. They were rigid, unyielding, and independent in their actions. Those schizophrenics who gave both self-assertive and compliant M's were, in the beginning, rigid and independent, but toward the end of the experimental situation they cooperated in order to accomplish the task. The majority of the schizophrenics who did not give any M's were self-assertive although some of them showed both self-assertive and compliant behavior.

The findings suggest the generalization that the quality of the M is directly reflected in the social role taking behavior when the person is ego involved in the social situation.

BIBLIOGRAPHY

1. Beck, S. J.: *Rorschach's Test*, 2nd Ed., Vols. I & II. New York: Grune & Stratton, 1950.
2. Ellenberger, H.: The life and work of Herman Rorschach. *Bull. Menninger Clin., 18:* 173–219, 1954.
3. Klopfer, B., and Sender, S.: A system of refined scoring symbols. *Rorschach Res. Exch., 1:* 19–29, 1936.
4. Klopfer, B., Ainsworth, M., Klopfer, W., and Holt, R.: *Developments in the Rorschach Technique.* Yonkers, N. Y.: World Book Co., 1954.
5. Meltzoff, J., Singer, J. L., and Korchin, S. J.: Motor inhibition and Rorschach movement responses: A test of the sensory-tonic theory. *J. Pers., 21:* 400–410, 1953.
6. Mirin, B.: The formal aspects of schizophrenic verbal communication. *Genet. Psychol. Monog.*, in press.
7. Phillips, L., and Smith, J. G.: *Rorschach Interpretation: Advanced Technique.* New York: Grune and Stratton, 1953.
8. Piotrowski, Z.: The M, FM, and m responses as indicators of changes in personality. *Rorschach Res. Exch., 1:* 148–157, 1937.
9. Piotrowski, Z.: A Rorschach compendium. *Psychiat. Quart., 24:* 543–596, 1950.
10. Piotrowski, Z.: Lectures. New York University, 1951.
11. Piotrowski, Z., and Schreiber, M.: Rorschach perceptanalytic measurement of personality changes during and after intensive psychoanalytically oriented psychotherapy, pp. 337–361. In: *Specialized Techniques in Psychotherapy.* Ed. G. Bychowski. New York: Basic Books Inc., 1952.
12. Rorschach, H.: *Psychodiagnostics.* New York: Grune & Stratton, 1942.
13. Schachtel, E. G.: Projection and its relation to character attitudes and creativity in the kinaesthetic responses. *Psychiatry, 13:* 69–100, 1950.
14. Singer, J. L., Meltzoff, J., and Goldman, G. D.: Rorschach movement responses following motor inhibition and hyperactivity. *J. Consult. Psychol., 16:* 359–364, 1952.
15. Singer, J. L., and Spohn, H. E.: Some behavioral correlates of Rorschach's experience-type. *J. Consult. Psychol., 18:* 1–9, 1954.
16. Werner, H.: *Comparative Psychology of Mental Development*, Rev. Ed. New York: Follet, 1948.

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VENOUS ANGIOMA AS A CAUSE OF CEREBRAL BIRTH PALSY[1]

A Review of 34 Cases Proved by Craniotomy

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This paper is being written with the express purpose of bringing before the medical profession a new concept of the pathology of cerebral birth palsy. In 34 children who have had craniotomy performed because of this condition, I have found cerebral venous angioma at the lower angle of the Sylvian fissure on one or both sides in 33 children. One boy with hydrocephalus had a subarachnoid cyst in the region of the cysterna magna, and one child had a subarachnoid cyst and venous angioma in the temporal region.

The clinical and pathological findings and their interpretation have been set forth and have previously been discussed by this author (1, 2).

Sharpe and Sharpe (3) showed, by lumbar puncture performed on 500 cases during the first 24 hours of life, that 9 per cent of children had evidence of intracranial bleeding. The bleeding may be due to one of many causes, such as prolonged birth, precipitate birth, hemorrhagic disease of the newborn, congenital vascular abnormalities, and prematurity infections of the nervous system.

The 33 children, who showed the cerebral venous angioma, ranged in age from under two years to 13 years. In each case, the vascular abnormality was found at, or near, the lower angle of the Sylvian fissure on one or both sides. The vessels may show a stellate form with the branches feeding into a central venous lake; they may take the form of a varicosity with veins feeding into a large, central vein; or there may be a pseudosinus formation. The sinus is usually circular, carrying venous blood, and surrounding an area of brain. The angioma may occasionally take the form of a series of small, parallel veins. The area encompassed by the vessels may be ½ inch by one inch to 2 inches by two inches. The skull usually shows a bluish tinge. The dura mater very often shows enlarged middle meningeal vessels. There are arachnoiditic adhesions of varying density in the region of the vascular abnormality, and, occasionally, the adhesions may tear a vessel when the dura is picked up. The brain in the region of the angioma is usually dusky red with a bluish cast and is often under pressure and non-pulsating at first. Sometimes, small arteries can be seen running over the surface of the venous angioma, which may make inroads into the brain to the depth of an inch or more.

An outline of the pertinent findings of each of the first 22 cases follows. However, the last 12 cases were operated upon recently, and so the results cannot yet be evaluated.

Case No. 1: P. A. A.—F, age 34 months, low forceps delivery, bilateral strabismus from 6 months of age, head is retracted and rotated to the left, convulsions began at 8 months, partially controlled by Dilantin and Phenobarbital, mentally defective, does not recognize parents, rigidity more marked on right side but spastic in all limbs, can swallow only strained food, cannot sit up by herself.

Left craniotomy: One year ago—cerebral venous angioma with adhesive arachnoiditis at lower border of Sylvian fissure. Angioma removed by electro-cautery. Can now walk with very little help. There is almost no spasticity, convulsions are rare, and has shown marked mental improvement and is beginning to speak.

Case No. 2: L. B.—M, age 3½ years—low forceps delivery, 80 to 100 convulsive seizures daily, began at 4 months, free of seizures with Mebaral since 8 months. Began to walk at 3 years, says "mommy", "daddy", hits head with hands frequently, Pneumoencephalogram read as "cerebral agenesis", cannot swallow solid foods. Walks with a tendency to sway to the right, spastic in all four limbs but more marked on the right, mentally retarded. Optic discs congested.

Left craniotomy: Venous angioma and arachnoiditis at lower border of Sylvian fissure. One months post-operation, the child swallows solid food, drinks milk from a glass by himself, no convulsions without medication. Little or no spasticity in limbs.

Case No. 3: M. A. B.—M, age 7½ years. Physician diagnosed cerebral hemorrhage the day after birth. Was cyanotic and kept in hospital in oxygen for three weeks after delivery. Sat up at 1½ years. Left-sided convulsions began at 5 years. Mental defective but can

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[1] This work was supported in part by the Parkchester General Hospital Fund.

say an occasional word, is destructive, left facial weakness (central type), spastic in all 4 limbs, spasticity more marked on the left, walks on wide base and uses right limbs better than left. Skull x-rays—suspicious of old linear fracture in right parieto-occipital region.

Left craniotomy: June 2, 1954—Small venous angioma at lower angle of Sylvian fissure cauterized.

Re-exam. June 24, 1954—Little or no spasticity. Motor power is improved, attention is better, looks more alert, speaks better. Oct., 1954—Patient had 2 convulsions in interval. Feb., 1955—No convulsions, with minimal medication.

Case No. 4: L. B.—F, age 28 months, dribbles saliva, cannot sit up by herself, mentally defective, cannot cry or make sounds, strabismus in left eye, spasticity in all limbs, slightly more marked on left. Skull x-rays show fracture of temporal region and along base of occiput. Shows evidence of pyknolepsy.

Left craniotomy: Feb. 1, 1955—Revealed venous angioma and arachnoiditis at lower angle of Sylvian fissure. Angioma cauterized. Has cried like a normal baby after operation. Is playful. Shows no spasticity or pyknolepsy and has definitely increased in motor power.

Case No. 5: D. J. B.—M, age 28 months, baby is RH neg., delivered by low forceps, cyanotic and drowsy at birth, with twitching of face and oculogyria, with inability to suck. Diagnosed as brain injury. Pneumoencephalograph, interpreted as "hypoplasia cerebri", shows excessive amount of air on right side. Convulsive seizures began at 6 months and consisted of 5 or 6 repeated attacks within a few minutes. Child is mentally retarded, aphasic, spastic in all four limbs, spasticity more marked on the left, cannot sit up, has stertorous breathing, cannot swallow solid foods, and has severe amplyopia.

Right craniotomy: Sept. 22, 1954—Subarachnoid cyst evacuated. Angiomatous vessels at lower angle of Sylvian fissure cauterized. Baby holds head better, moves across bed, laughs, greatly diminished spasticity, and sees better. Increase in motor power.

Case No. 6: A. R. B.—M, age 9 years, forceps delivery. Cyanosis at birth and 6 months thereafter. Sat up at 14 months, mentally retarded, aphasic, severely amblyopic, began to walk at 6 years, moderately spastic in all four limbs, with more spasticity on the right side. Skull x-rays show increased vascular markings on the right side. Keeps hitting his head as if in pain.

Right craniotomy: Oct. 26, 1954—Venous angioma at lower angle of Sylvian fissure cauterized.

Jan., 1955—Child is more observant, bathroom trained, eyesight is improved, and tries to speak.

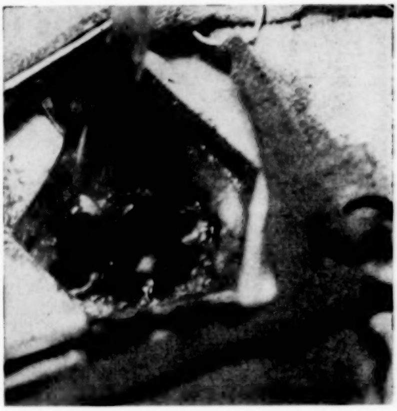

FIG. 1. Venous angioma before cauterization.

Case No. 7: K. D.—M, age 7 years. Delivered by forceps. Born with 6 fingers and 6 toes on one foot. Testicle undescended. Diagnosed as spastic at two weeks of age. E.E.G. shows epileptic pattern. Diagnosed in a children's hospital in another city as arrested hydrocephaly with mental retardation. Sat up at 5 years of age, can say a few words and makes his wants known. Spastic in all limbs, dribbles saliva constantly, focal attacks involving right upper limb began at two years of age, similar attacks about every 3 months. Has been controlled with Tridione since 1952. Strabismus and oculogyria, severe.

Left craniotomy: June 2, 1954—Revealed large venous angioma with arachnoiditis at lower angle of Sylvian fissure. This was cauterized.

Sept., 1954—Intelligence is improved, beginning to speak, better motor power, markedly diminished spasticity, eyes focus better, but has had convulsive seizures in July and in September. Has not returned for further follow-up.

Case No. 8: B. A. E.—F, age 3 years, 10 months. Had been unable to take milk from nipple at birth, sat up at 8 months. Mentally retarded, does not speak, focal convulsions involving left arm and left side of face, began in 1953, spasticity in all limbs but more marked in left limbs. Skull x-rays show fracture of the base. Pneumoencephalogram shows pocket of air in right fronto-temporal parietal region.

Right craniotomy: June 8, 1954—Cauterization of venous angioma at lower angle of Sylvian fissure.

Aug., 1954—Head is larger, baby is more intelligent, tries to say words, spasticity almost completely gone. No convulsive seizures. Improvement in motor power.

Case No. 9: J. F.—M, age 13 years—delivered by "instruments". Had to be fed by eyedropper for a few weeks. Sat up at 6 years. Focal convulsive seizures began at 5 years. Left eye and head would turn to the left during an attack. Intelligence is normal. Athetotic movements of head and all limbs, with marked rigidity in right upper limp. Unable to speak but understands everything. Has difficulty in swallowing and in breathing.

Left craniotomy: Aug., 1954—Circular venous sinus at lower angle of Sylvian fissure cauterized.

Nov., 1954—Has been improving steadily. Can stand at table for a few minutes. Spasticity and athetosis greatly diminished. More control of movements. Can say a few words. Breathes and swallows without

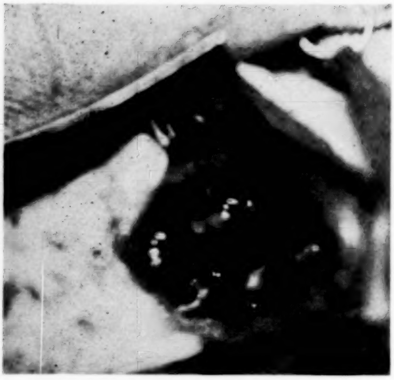

FIG. 2. Venous angioma before cauterization.

difficulty. Feb., 1955—Has been typing words on an electric typing machine.

Case No. 10: J. E. G.—F, age 2½ years. Severe jaundice at birth. Right hand was useless at first. Cannot sit up, aphasic, mentally retarded. No convulsive seizures. Spasticity in all four limbs, more marked on the right side.

Left craniotomy: Jan. 27, 1954—With cauterization of venous angioma at lower angle of Sylvian fissure.

Jan., 1955—Baby walks with very little support. Almost no spasticity. Is toilet trained. Makes all her wants known and is beginning to speak. Aug., 1955—Can walk without support.

Case No. 11: G. K. Jr.—M, age 2½ years. Cerebral palsy with rigidity in all four limbs with head retraction. History of RH neg. blood type. Complete blood exchange at birth. Diagnosed as cerebral palsy at age of 7 months. Baby cannot hold head up, is mentally retarded, and has been suffering from epilepsy since the age of 7 months.

Nov. 10, 1953—Left fronto-parietal craniotomy revealed adhesive arachnoiditis and angiomatous vessels at lower angle of Sylvian fissure. Cauterized. Reexplored on Nov. 11, 1955, because of focal convulsive seizures. No bleeding found. On Dec. 4, 1953—Herniation cerebri. Oct. 23, 1954—Knows his family. Watches television. Swallows better. Breathes better. Can hold his head up and move about. Spasticity gone. No convulsions. Herniation covered by skin.

Case No. 12: S. K.—M, age 6 years. Mother RH neg. Child jaundiced at birth. Athetotic-spastic paralysis in all limbs. Cannot sit up, is aphasic and mildly mentally retarded. No epilepsy. Spasticity more marked on the right side. Skull x-rays show marked vascular erosion in left fronto-temporal region.

July 1, 1954—Left craniotomy with cauterization of angioma at lower angle of Sylvian fissure. July 13, 1954—Child tore open wound and got a cerebral hernia. Feb. 19, 1955—Child has more control of movements and better motor power. Beginning to say some words. Put on weight. Spasticity and athetotic movements almost entirely gone. Herniation gradually retrogressing and covered by skin. June, 1955—Drainage of cerebral abscess. Aug., 1955—Child died after recurrence of cerebral abscess.

Case No. 13: T. K.—F, age 4½ years. Neurologist called at birth—reason not known. Has trouble swallowing and breathing. No convulsions. Tries to sit up. Has some moderate mental defect. Spasticity in all 4 limbs, more marked on the right. Child is aphasic. Skull x-rays show marked vascularity in right frontal region.

Nov. 11, 1954—Venous angioma at lower angle of right Sylvian fissure cauterized. Dec. 11, 1954—Gained weight. Swallows better. Is brighter. Holds head better. Uses hands better. Spasticity greatly improved. Aug., 1955—Improvement in motor power and intelligence.

Case No. 14: S. L.—F, age 18 months. Convulsions at 7 months following upper respiratory infection. Since then, has had multiple petit mal attacks—as many as 100 per day. Had typhoid therapy. Rigidity in all four limbs. Cannot sit up, cannot recognize parents, is severely amblyopic and convulsions are becoming generalized.

Mar. 13, 1954—Right craniotomy—non-pulsating, cyanotic brain with angiomatous vessels at lower angle and Sylvian fissure. Abnormal vessels cauterized. Sept. 18, 1954—No convulsions or petit mal since operation. Can stand by herself. Laughs and plays with sister. No spasticity. Dec. 14, 1954—Climbed into bathtub and was drowned.

Case No. 15: D. M.—M, age 27 months. Premature and jaundiced at birth. Had measles at 4 months. Inguinal hernia repaired at 2 years. Spasticity noticed at one year. Spastic in all 4 limbs, shows bilateral strabismus and severe amblyopia. Cannot hold head up, cannot swallow solid foods. Generalized convulsions came on one week before consultation. Shows pallor of optic discs, mental retardation is severe. Skull x-rays showed abnormal vascular markings at left pterion.

July 28, 1954—Left craniotomy with cauterization of angioma at lower angle of Sylvian fissure. Sept. 2, 1954—Swallows better and spasticity greatly improved. Breathing is easier. Can sit up with support. Eye movements are more coordinated. Baby laughs and is playful now. No convulsions.

Case No. 16: W. A. M.—, 9 years. Precipitate birth. Cyanotic at birth. Jerking of limbs after birth persisted for months. Projectile vomiting. Strabismus, bilaterally. Has multiple petit mal attacks daily. Walks up stairs with his right leg and pulls left after him. Spasticity more marked in left limbs. Can walk and use kitchen utensils. E.E.G. shows generalized dysfunction. Skull x-rays show "silver mottling" with increased vascular markings on the right side.

Feb. 5, 1955—Right craniotomy revealed venous angioma which was cauterized. Also there was a gliotic scar in the region of the lower angle of the Sylvian fissure. Bone of skull was excessively thick and marblized. Mar. 1, 1955—Speaks words, better behaved, attention is better, no petit mal attacks since operation. Walks better, no spasticity.

Case No. 17: P. J. R.—F, age 3 years. Premature birth—kept in hospital for 3 months after delivery. Cannot hold head up and is mentally retarded and aphasic. Spastic in all limbs, more marked in left limbs. Cannot breathe properly. Spinal tap—242 mm. H_2O pressure. Skull x-rays showed "silver mottling".

Nov. 18, 1953—Left craniotomy—adhesive arachnoiditis in region of lower angle of Sylvian fissure with venous angioma. Adhesions separated and angioma cauterized. May, 1954—Improvement in motor power and cerebration. Can say some words. Spasticity almost completely gone.

Case No. 18: P. J. S.—M, age 2½ years. Attacks of laryngeal spasm and choking since 11 months of age. Intracranial pressure—18 mm. Hg on spinal tap. Skull larger than normal. Diagnosed as partial block of 4th ventricle at a University Hospital. Cannot hold head up, rigid in all four limbs. Mental retardation—mild to moderate.

Oct. 27, 1953—Suboccipital craniotomy. Adhesive arachnoiditic cyst obstructing 4th ventricle. Died about 6 days post-operation. Anatomical cause of death—bronchopneumonia. Brain showed cortex and white matter to be grossly normal although the lateral and third ventricles were moderately dilated.

Case No. 19: L. S.—F, age 2 years—one of a twin—other child normal. Convulsive seizures began at 4 months. Has been controlled by a barbiturate for the last year. Child is mentally retarded, aphasic, mildly microcephalic, cerebro-spastic in all limbs, and amblyopic. Cannot hold head up.

Left craniotomy: Aug., 1954—Venous sinus at lower angle of Sylvian fissure cauterized and arachnoiditic adhesions separated. Dec. 20, 1954—Swallows better. Eats better. Beginning to turn over by herself. No spasticity. Uses limbs better. Seems to have improved eyesight. No convulsive seizures.

Case No. 20: D. R. S.—F, age 3 years. Doctors told mother that the baby was injured at birth—had oxygen, blood transfusion and calcium injections. Lumbar puncture after birth revealed hemorrhagic C.S.F. Child has a moderate amount of intelligence, lets her wants be known and understands everything. She shows severe athetotic type of cerebral palsy. This involves her head and all her limbs. Swallowing and breathing are difficult. No epilepsy. Aphasic.

Nov. 3, 1953—Left craniotomy—venous angioma at lower angle of Sylvian fissure cauterized. Arachnoiditic adhesions separated. Right craniotomy—same date—showed dense arachnoiditic adhesions which were difficult to separate from cortex which showed a gliotic scar. Jan., 1954—Patient still spastic and athetotic but can sit quietly in her chair for longer periods. Swallows and breathes better.

Case No. 21: A. G. T.—M, age 9½ months. Premature birth—breach delivery—?forceps. Baby "collapsed" that night and was transferred to another hospital—diagnosis of intracranial hemorrhage and pneumonia was made. Baby cannot sit up—fontanelles are closed. Skull slightly smaller than normal. Paralysis of left upper limb.

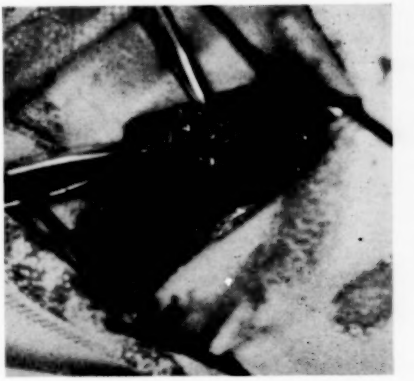

FIG. 3. Venous angioma before cauterization.

Oct. 27, 1953—Right craniotomy revealed massive angiomatous vessels in and about the Sylvian fissure. These were cauterized. Skull was full of venous sinuses. Oct. 28, 1953—Patient re-operated for bleeding from bed of cauterized angioma. Baby died about four days post-operation. Anatomical cause of death—cerebral edema. Cortex and ventricles were grossly normal.

Case No. 22: A. W.—age 6 years, male. No difficulty at delivery. Vomited his feeding constantly and kept crying without apparent cause. As he grew older would often hit his head as if in pain. Sat up at 2 years. E.E.G. showed generalized pressure type of wave. Diagnosis at a University Hospital in another city was cerebral palsy with marked mental deficiency. Showed microcephaly with "turm schadel". Athetotic movements of limbs—mild. Can pull himself onto his feet but cannot walk without support and only a few steps with support. Epilepsy began at 2 years. Had a few attacks daily. There was a focal quality to the attack. Lately, the attacks are controlled by large doses of Phenobarb. Aphasia—motor and sensory type.

Jan. 3, 1954—Left craniotomy—adhesive arachnoiditis and venous angioma at the lower angle of the Sylvian fissure. Adhesions separated and angioma was cauterized. Oct. 22, 1954—Had an attack of measles with convulsions. Can stand and walk better. Pays more attention to toys. Can open jars and turn on television. Taken off Dilantin and has had no further convulsions since his fever (measles and virus infections).

The most recent 12 cases consisted of 9 females and 3 males. All these children were cerebro-spastic, mentally defective, and epileptic. 10 of the children had grand mal seizures. One female child had petit mal attacks. 2 children developed bronchopneumonia after a number of days. They died as a result of this disease. The post-mortem findings confirmed the diagnosis of bronchopneumonia. The brains were grossly

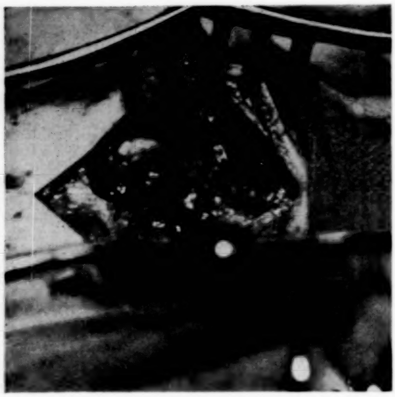

FIG. 4. Venous angioma after cauterization.

within normal limits. The operative site had completely healed. The ten remaining children are all somewhat improved in that their spasticity is greatly diminished, epileptic attacks are either diminished or have not returned, and some have shown more alertness. All 12 children showed venous angioma at the lower angle of the Sylvian fissure at operation.

CONCLUSIONS

The concept of a cerebral cause for cerebral palsy is self-evident. However, the neurosurgeons, except for W. Sharpe, have done little, or nothing, to help these unfortunate children or their parents. This does not take account of the work that is being done on adults.

In this series of cases, 34 children have undergone craniotomy. Sixteen were male; 18 were females The youngest was 9½ months, and the oldest was about 13 years of age. One child had a bilateral craniotomy.

Clinical signs and symptoms. Those exhibited in these cases were cerebral paralysis usually of all four limbs of the spastic or athetotic type, mental deficiency in almost every case, inability to hold head up or sit up, strabismus in one or both eyes, amblyopia, drooling of saliva in about half the cases, difficulty in swallowing, difficulty in respiration with stertorous breathing, and epilepsy. The epilepsy may be of the pyknotic variety, petit mal, focal or generalized type.

Causes of cerebral palsy in this series of cases. Birth injury by precipitate delivery, prolonged labor, instrumental delivery, hemorrhagic disease of the newborn, blood dyscrasia and possible encephalitis in one case.

Basis for operation. The child must have physical disability with little or no progress with medication or rehabilitation. Mental disability and epilepsy should be no deterrent to operation. In fact, the epileptic picture may often give an indication as to localization. If the child shows that the spasticity is more marked on one side, and most of them do, then mental defect should not stand in the way of operation.

Skull x-rays will often give an indication as to which side should be exposed at operation. The venous channels will be more marked on one side, and, occasionally, one will find a venous sinus in the region of the pterion on one side. After all the evidence is weighed, then the side for craniotomy is chosen. Sometimes, only minimal evidence is available for aid in making this decision, in such a case the left side should be done in children who come from a right-handed family. Often, there is no indication of "handedness" in these children.

Craniotomy. A linear incision is made three inches long, centered over the pterion and running in the coronal plane. The skull often is definitely of a bluish cast. The skull is opened to the size of a silver dollar. The dura may be normal, or may also seem to have a bluish discoloration. Occasionally, the middle meningeal veins are enlarged and tortuous. These vessels are cauterized. The dura is opened in a stellate manner. However, one should be very careful in lifting the dura for the arachnoiditic adhesions may tear into a venous sinus or enlarged vein. The angioma is found in relation to the lower angle of the Sylvian fissure. It may be one of three varieties: (a) A venous sinus which may take any shape and occasionally is circular. (b) A venous lake with tortuous enlarged vessels feeding into it and small arteries running over the surface of it. (c) One or more enlarged veins feeding into a central vein.

The brain is of a reddish blue color and is at first non-pulsating. There are arachnoiditic adhesions in relation to the angioma and usually very little flow of cerebrospinal fluid. The brain may begin to pulsate immediately after the dura is opened and sometimes pulsates while the dura is being opened.

After the angiomatous vessels are cauterized with the electrocautery, the brain will become pinkish-red within a number of minutes. After bleeding is controlled, the temporal muscle is closed, but dura mater and temporal fascia are not closed. Skin and temporal muscle are repaired by separate silk sutures.

Mortality. Two children died a few days post-operatively. Cerebral edema was the cause of death in one and bronchopneumonia in the second. A third death was due to recurrent brain abscess about 14 months after operation. The fourth and fifth deaths were due to bronchopneumonia after operation.

Complications. Two children tore open their incisions at home, and brain herniation resulted. One child had spontaneous repair. The other child developed a brain abscess which was surgically drained and then recurred. This child died two months after surgical evacuation of pus when abscess recurred.

SUMMARY

One case of subarachnoid cyst with venous angioma at the region of the pterion, one case of subarachnoid cyst in the posterior fossa, and 32 cases of venous angioma in the region of the pterion were found in 34 cases of cerebral palsy which came to operation.

In the 29 children who survived operation, all improved. Some of the children improved slowly and only in small things, such as muscle control, muscle power, diminished spasticity. All who had difficulty in swallowing and breathing overcame these difficulties. All who had amblyopia showed some improvement. Spasticity was always diminished and so was athetosis. Epilepsy never returned in the majority of children and was definitely diminished in others. Strabismus was improved or completely gone after operation. Drooling was diminished in most cases.

Mental status was improved so that in some cases the children began to say words, became playful, and showed signs of active intelligence. Some children are beginning to walk who could not sit up by themselves before operation. About eighteen months have passed since the first child was operated upon. Within this short period of time, all have shown some progress, and some have shown remarkable progress.

Rehabilitation has an important place in the post-operative care of these cases, for the operation only makes these children more amenable to rehabilitation. Marked improvement should be possible in a majority of cases over a prolonged period. Glandular extracts of pituitary and thyroid and vitamins B1, B6, and B12 play an important part in post-operative care.

It is my opinion that the pathology is definite and that it indicates a means of attack which has helped these children. The procedure is deserving of further trial.

BIBLIOGRAPHY

1. Rosner, S.: Neonatal bleeding and cerebral birth palsy. *J. Internat. Coll. Surgeons, 19:* 494, 1953.
2. Rosner, S.: Venous angioma: A cause of cerebral palsy. *J. Internat. Coll. Surgeons, 22:* 94, 1954.
3. Sharpe, W., and Sharpe, N.: *Neurosurgery: Principles, Diagnosis and Treatment,* pp. 100–146. Philadelphia: J. B. Lippincott Company, 1928.

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METHODOLOGICAL ASPECTS OF PSYCHIATRIC RESEARCH IN HANDWRITING

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Onset of Scientific Research in Handwriting

The handwriting of mentally ill patients has been subject to attention and study since Kraepelin (13) who noticed and investigated fundamental changes of the writing pressure in scripts of psychotic individuals. He and his pupils used specially designed writing scales for measuring writing pressure. Kraepelin's methods were improved by Goldzieher-Roman (4, 5, 6) who first worked in handwriting research in Budapest and has continued in this country. Saudek (22) is another investigator in this field, and new apparatus were developed in Kretzschmer's psychological laboratory (24, 25, 26) in Wuerzburg by Steinwachs for testing writing pressure, grip pressure and writing speed in different groups of individuals.

Kraepelin's work can be designated as the beginning of scientific investigation in the problems of handwriting. This type of handwriting analysis is entirely different from the intuitive-artistic way which the so-called graphologists practise it. They try to form an opinion on somebody's personality by examining form and movement of writing. Both methods have advantages and disadvantages.

Advantages and Disadvantages of Experimental Handwriting Research

Kraepelin's methods are of an experimental nature. The advantage of such a method is the possibility of obtaining results by measurement in quantities which can be expressed in figures, and figures are comparable. The experimental or quantitative method, therefore, is statistically oriented and gives the results with a maximum of certainty and exactitude for a predetermined observation.

The disadvantage of this method of examining handwriting lies in the fact that a test situation is unavoidable which may influence the behavior so that it may become quite different from the natural behavior of the test subject. An individual might even be unwilling to undergo such a test. Valuable results may then be unobtainable or become distorted. This applies especially to psychotic patients who are often too suspicious and delusional to coöperate. Therefore, the quantitative method has its limits. In order to obtain representative results, investigations by this method have to be carried out on large groups of persons, and the results can be evaluated only in terms of the whole group and not of individuals composing the group. For instance, Goldzieher-Roman measured with the "Graphodyne", a highly sensitive device, pressure and speed in writing of more than 2,000 normal school children and of several hundred maladjusted children, among them, left-handers, stutterers, deaf-mutes, as well as children of known asocial behavior, for comparison. The results, of course, were typical and significant for a whole group but not for an individual of that group. Therefore, it would not always be possible to judge from the measured value in a single case to which group he belongs.

Another disadvantage of the quantitative method in handwriting examination is the rigidity of the method. The character of the observation is, as mentioned above, predetermined. This will lead to a rigid and inflexible investigation which often might be inappropriate or insufficient in the individual case. For instance, suppose it is planned to measure the writing pressure, but a first glance at the script may already tell that the specimen to be examined reveals strange or exaggerated forms and that concentration on them may give us much better information than measuring of the writing pressure.

A third disadvantage of the experimental method is that experimental handwriting analysis usually depends on equipment which is either expensive or not easily available.

ADVANTAGES AND DISADVANTAGES OF THE METHOD OF THE CLASSICAL GRAPHOLOGY

The disadvantages of the experimental handwriting research are the advantages of the classical graphology. First there is no test situation at all. Specimens, not written for the purpose of the test but for some other occasion, are analyzed. In this way spontaneously written material can be used which may be very revealing as to the variable emotional reactivity of the writer in response to different stress situations. Since in the classical graphology the experimental test is excluded, handwriting specimens, produced by the same individual some time in the past, can be used too and may give valuable information from the psychodynamic point of view when compared with specimens written later. This possibility could be utilized especially if a patient is uncooperative or unwilling to undergo psychological testing.

Another advantage of this method is the strictly individual significance of each analysis; e.g., a certain feature in writing was observed in a group of individuals who behaved equally in a certain way. If the same characteristic is found in the writing of an individual outside the original group, it is assumed that the person in question shows the same special type of behavior as the individuals of the original group. This method of thinking, forming conclusions by deduction, is defensible because it has proved useful in many branches of science, especially in medical research. But the deductive method, applied to handwriting analysis, has great dangers as we will see later.

The third advantage of the classical graphology is the adaptability of the method to the individual specimen. In this way one can concentrate on the preponderant features of a script; for instance, a handwriting, the most conspicuous features of which are a supernormal height and a supernormal narrowness of the middle zone letters, would call for concentration on these features (see figure 1).

As the fourth advantage of the classical method in graphology, it should be mentioned that no instrumental equipment is needed for this kind of analysis. The analyst depends entirely on his ability to recognize the most conspicuous characteristics in a handwriting and on his knowledge and experience of appropriate interpretation.

But these advantages of the classical graphology are countered by two important disadvantages. Since this method is not at all or only to a minor degree based on quantitative investigation, the rules of the classical graphology are quite vague and subject to speculation, features which rendered this method suitable for fortune teller practice. Charlatans found an opportunity to use the methods of the classical graphology for the exploitation of the common naïve curiosity in the other person's character. In this way the term, graphology, became afflicted with the derogative meaning of a pseudo-science. Therefore, many serious investigators felt repelled by these technics and did not dare to look deeper into the problems of graphology. A resistance to the word and meaning of graphology developed, and this discipline became the stepchild in psychodiagnostics.

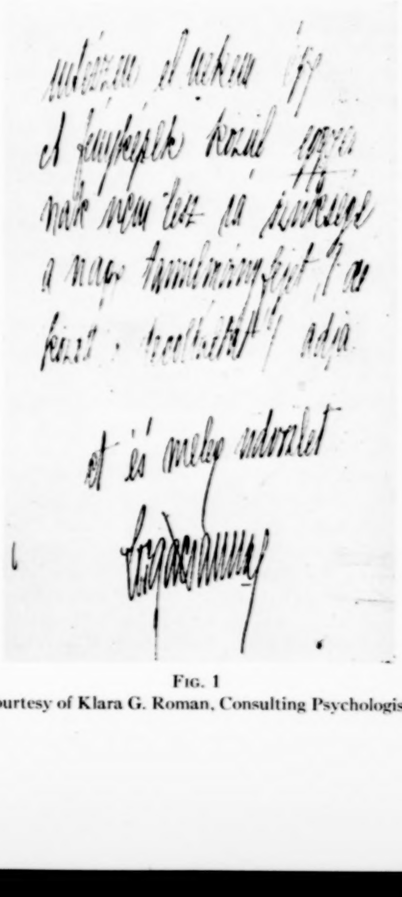

FIG. 1
(Courtesy of Klara G. Roman, Consulting Psychologist)

But interest in this matter has never ceased to exist among well-known psychiatrists and psychologists. One of the reasons for it must have been the unrefutable fact that handwriting is specific and typical for a certain individual. Therefore, a number of serious scientists declared frankly their interest in the meaning of expressive movements as revealed by handwriting. We mentioned the names of Kraepelin and Kretzschmer. Bleuler (1) also has to be named who gave a series of typical illustrations of handwriting in mental patients.

One may argue that Bleuler, Kraepelin and Kretzschmer were never engaged in the way of handwriting analysis as the classical graphology indulges. But even if they did not practise research of this kind themselves, they have *nolens volens* pointed in this direction because they recognized the importance of handwriting as a projection of behavior and personality.

The interpretation of a handwriting by conclusions, formed on the basis of empirical observation, as it is done in the classical handwriting analysis, is a method of thinking which is quite common in medical science too. Almost our entire physical diagnosis is based more on thorough empirical observation and experience than on quantitative-statistical investigation; for instance, auscultation and percussion of heart and lungs are methods developed and first applied by brilliant observers and thinkers on a strictly empirical basis and personal experience. If we should doubt the practical value of these methods as guidance to diagnosis, especially under circumstances when other diagnostic methods are not immediately available, we would devaluate precious tools and undermine the fundaments of modern medical diagnostics. The late O. Naegeli in Zurich, an outstanding clinician, very familiar and working successfully with deductive-quantitative methods, even recommended in his lectures diagnosis from certain structures of the nails. We know well that there is no quantitative-statistical material available yet to give this kind of diagnostic method a generally recognized basis. On the other hand, if such a method is recommended by an excellent scientist, one will be inclined to show an open mind towards his suggestion.

The same attitude should be shown to classical graphology which was developed and successfully applied by seriously-minded scientists like Klages (7, 8, 9, 10, 11, 12) and Pulver (18, 19, 20) and continued in this country by psychologists like Wolff (29, 30), Goldzieher-Roman (21), Sonneman (23), and others. Lately, Malford W. Thewlis, a well-known physician (author of "Care of the Aged"), published in collaboration with Isabelle Clark Swezy an interesting book, dealing with the emotional states, projected in handwriting (27). Thewlis and Swezy still pay some attention to the interpretation of single signs which was originally emphasized by the French author Michon (15, 16, 17) and is likely to be more and more discarded now; but they are aware of the advancement in modern graphology and gave a constructive contribution. Michon's evaluation of single signs should not be entirely discarded. It may still be useful if the original aspect is widened. This leads us to the second difficulty of classical graphology.

Handwriting is a Gestalt phenomenon. Only the totality of forms and movements all together creates the impression which will eventually lead to the right diagnosis of the writer's personality. If we dissect this impression in detailed signs and characteristics and try to evaluate them separately, we will frequently arrive at a distorted image of the writer's personality. Klages tried to overcome this difficulty by assigning each handwriting characteristic a positive and a negative meaning. Whether the positive or the negative meaning applied in an individual case depended on the form-level of a script. Form-level was understood by Klages as the degree of originality and esthetic balance which only could be perceived by intuition. It is clear that this was a vague criterion which, however, had many followers. It was revived lately in an interesting book by Ulrich Sonneman (23). The majority of modern graphologists rejected the criterion of form-level as too subjective and unreliable and preferred to concentrate on the combination of the predominant features in a script. It seems that this way allows more objective control and is much closer to reality than the Klages concept which can open the door to speculation.

Being aware of the disadvantages of Klages' method, Goldzieher-Roman as well as Thewlis and Swezy prefers the method of combinational interpretation of signs and features. Two examples from G.-Roman's excellent book (figures 1 and 2) and two specimens, written by patients of the VA Hospital, Canandaigua, New York, (figures 3 and 4) may illustrate the meaning of this method.

Figure 1 shows the writing of a woman, 20 years of age. Predominant features are brittleness of stroke, extreme narrowness and immoderate height of the middle zone letters in relation to the upper zone letters, and overextension of the lower zone letters. The writer, a victim of a killer, was a pretentious narcissistic-masochistic character who chose a brutal mate as an instrument of her unconscious need for self-destruction.

The writing in figure 2 is the "old-fashioned script of a nineteenth-century bride-to-be addressing her future husband". The specimen shows flooded ovals, swoops and swellings which normally are observed during puberty. According to G.-Roman, in an adult they may point to immaturity and emotional disturbance, especially in relation to sex. The writer later was found to be schizophrenic. Her offspring was mentally deranged too.

Figure 3 is the writing of a 57-year-old psychotic patient suffering from residuals of polioencephalitis. Notice the exaggerated capitals, the swoops at their beginning and end, the ugly and rigid leftward loops of y and g, the trembling in many up-and-down strokes, the improper spacing between letters and the sudden enlargement of the e and two s' in "Happiness". This patient displays delusions of happy grandeur. He thrones on the couch like a sultan on his divan, imagines he is the Lord and greets everybody with a smile.

Figure 4 represents the writing of a paranoid schizophrenic, 65 years of age. He also has delusions of grandeur and thinks of himself as a great musician and composer. He makes a fair adjustment in the hospital where the personnel do not contradict him. On the outside he finds it very difficult to get along with people who, he thinks, do him injustice and persecute him. A marked rigidity in his writing with leftward slant, extreme pressure, flooded ovals, embellishments on the top of exaggerated capitals, balloon-like lower loops, low middle zone letters are conspicuous.

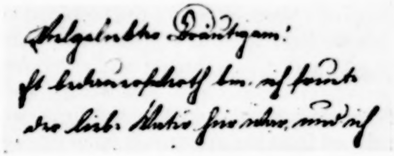

FIG. 2

(Courtesy of Klara G. Roman, Consulting Psychologist)

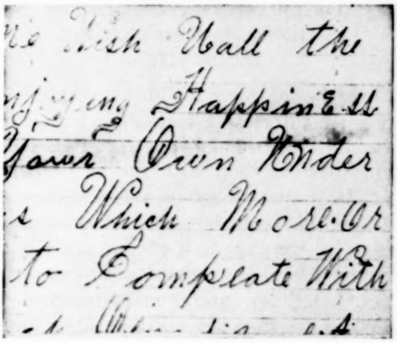

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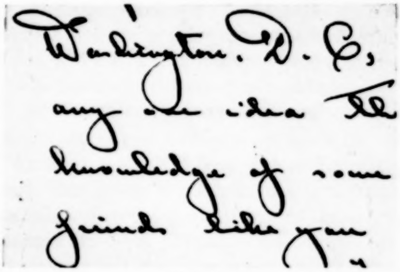
FIG. 3



Washington. D. C.,
knowledge of some
friends like you

FIG. 4

The above examples may demonstrate the value of combinational interpretation of the predominant characteristics. K. G. Roman suggests in her book (21) to use a worksheet for listing them. This method can be especially recommended to beginners. But as she points out too, even as we find interesting co-variations between handwriting features and behavior pattern, until now we are still in need of a statistical verification of the findings. Therefore, all interpretations of handwriting specimens are to be taken with caution and reserve. Until this verification is obtained, a personality evaluation only on the basis of handwriting should be impermissible on ethical and scientific principles. But in this pre-scientific stage handwriting analysis already may render some help in reaching a diagnosis. Especially, as Victor (28) points out, it may help to gain more information in a single case concerning instinctual drives.

To give a short review of the problems cited so far, we have tried to explain briefly the advantages and disadvantages of the inductive-experimental research in handwriting and of the classical graphological procedures which developed from the interpretation of signs over the bi-polar form-level evaluation to the modern combinational technic.

Onset and Development of Gestalt's Research in Handwriting

From the foregoing the idea is very close: Is it possible to create a method in handwriting research which combines the advantages of the quantitative method with the advantages of the classical graphology by avoiding the disadvantages of both methods? Lewinson and Zubin (14) were the first ones to try this on a scientific level. They developed a system of scales, based on careful measurements with especially designed devices of basic features in scripts to determine every handwriting movement in the horizontal, vertical and depth direction. This was a very time-consuming procedure, and since only single words were measured, it seems impossible that such a method could exhaust the probably vast possibilities which a whole handwriting pattern offers. This also applies to Wolff's ingenious method, elaborated in his book (30), to measure the longitudinal extensions of given and family name and to calculate proportions between these figures. By studying only the signature we would not penetrate into the Gestalt of a handwriting.

Therefore, we tried another approach to the problem. The question was, how to determine Gestalt features of handwriting? But what is Gestalt of handwriting? It is the objective esthetical impression, imparted by the totality of forms and form-relationships in a script. The forms are created by the individual way of moving a pen over blank spaces of paper. In this manner a page of writing appears to be divided into lines, words, partial words, margins on the left and the right, and blank spaces between words, lines and parts of words. If we measure these forms and calculate ratios among them, it is possible to formulate a quantitative expression of the Gestalt of a script in figures. The problem was, how can we perform such measurements in a simple and fast way, avoiding the above-mentioned disadvantages of Lewinson and Zubin methods? For instance, if the ratio of the horizontal extension of words to the total length of lines is to be determined, all words have to be measured and the single figures added before this ratio can be calculated. Using an inch scale for this procedure would be too time-consuming and impractical. Therefore, as we described in a previous paper (2), we measured the horizontal extension of the words with a map measure. This simple and inexpensive device helped us to perform the measuring of an average page in about three minutes, and since this is an integrating instrument, we obtained automatically the total figure of all the horizontal word extensions at the end of the procedure. For more details of this method the reader may be referred to the original paper.

It may only be mentioned here that in handwriting specimens of physically and psychologically stable individuals, we obtained ratios which were not significantly different from certain mathematic-esthetic figures, originally discovered by Euclid and called the ratio of the "Golden Section" (3). This might sound strange at first. However, if we realize that certain mathematical proportions can easily be demonstrated in the way nature likes to construct generally (which allows to identify different species in both the organic and inorganic world), it would be strange if there were no definite form principles detectable in handwriting. More methods for investigation in this direction can be developed. They will open new interesting aspects in handwriting research which may lead to valuable information on personality. Coming to the end of this outline on the methodological problems in handwriting research, we recapitulate briefly.

Summary

Three methods of handwriting research were discussed and their advantages and disadvantages pointed out:

1. Methods of quantitative experimental research. We recall Kraepelin's method, his introduction of the writing scale.
2. The classical graphological method, starting out with the interpretation of signs, developing over a bi-polar evaluation of signs and movements to the modern combinational way of handwriting interpretation.

3. Actual measuring of handwriting characteristics, leading to penetration in the Gestalt of handwriting by quantitative methods, and the evaluation of the results from the mathematic-esthetic point of view.

The third method, if further developed and enriched by complementary methods, will eventually help to pave the way for a better and wider appreciation of handwriting research as a valuable tool in psychodiagnostics.

I wish to express my sincere thanks to Dr. L. V. Lopez for making this paper possible and to Prof. Dr. J. Romano and Dr. D. Davis for reading the manuscript and for their suggestions. I also am much obliged to Dr. K. Messing for providing an interesting handwriting specimen of a patient on his ward and to Klara G. Roman for her permission to reproduce two pictures from her book.

BIBLIOGRAPHY

1. Bleuler, E.: *Lehrbuch der Psychiatrie.* Berlin: Julius Springer, 1943.
2. Bruck, M. A.: Contribution to the survey of handwriting. *Am. J. Psychiat., to be published.*
3. Euclid II: 11, See "Golden Section" explained in Webster's New International Dictionary, 2nd Ed., 1952.
4. Goldzieher-Roman, K.: Graphodyn. *Zeitschrift f. angewandte Psychologie, 11:* 23–33, 1931.
5. Goldzieher-Roman, K.: *Az irás kisérleti vizsgálata* (Experimental Investigation of Handwriting). *Jövö utjain,* no. 2, 1934.
6. Goldzieher-Roman, K.: Studies on the Variability of Handwriting: The Development of Writing Speed and Point Pressure in School Children. *J. Genetic Psychology, 49:* 139–60, 1936.
7. Klages, L.: *Die Probleme der Graphologie.* Leipzig: J. A. Barth, 1910.
8. Klages, L.: *Ausdrucksbewegung und Gestaltungskraft.* Leipzig: J. A. Barth, 1913.
9. Klages, L.: *Einfuehrung in die Psychologie der Handschrift.* Stuttgart: W. Seifert, 1924.
10. Klages, L.: *Der Geist als Widersacher der Seele.* Leipzig: J. A. Barth, 1929.
11. Klages, L.: *Die Grundlagen der Charakterkunde,* 8th ed. Leipzig: J. A. Barth, 1936.
12. Klages, L.: *Handschrift und Charakter,* 18th ed. Leipzig: J. A. Barth, 1940.
13. Kraepelin, E.: *Psychologische Arbeiten.* Leipzig: Engelmann, 1898
14. Lewinson, T., and Zubin, J.: *Handwriting Analysis.* New York: King's Crown Press, 1942.
15. Michon, J. H.: *Les mystères de l'écriture.* Paris: 1872.
16. Michon, J. H.: *La methode practique de graphologie.* Paris: Payot, 1878.
17. Michon, J. H.: *Histoire de Napoléon Ier d'après son écriture.* Paris: 1879.
18. Pulver, M.: *Trieb und Verbrechen in der Handschrift.* Zurich: Orell Füssli, 1934.
19. Pulver, M.: *Symbolik der Handschrift,* 3rd ed. Zuerich: Orell Füssli, 1940.
20. Pulver, M.: *Der Intelligenzausdruck in der Handschrift.* Zuerich: Orell Füssli, 1949.
21. Roman, K. G.: *Handwriting: A Key to Personality.* New York: Pantheon, 1952.
22. Saudek, R.: Zur psychodiagnostischen Ausdeutung des Schreibdruckes. *Zeitschrift f. angewandte Psychologie, 39:* 433–449, 1931.
23. Sonneman, U.: *Handwriting Analysis.* New York: Grune & Stratton, 1950.
24. Steinwachs, F.: Die verfeinerte mechanische Schreibwaage. *Archiv f. Psychiatrie und Zeitschrift f. Neurologie, 187:* 521–536, 1952.
25. Steinwachs, F., and Kluge, E.: Schreib-psychomotorische Veraenderungen in Hypnosis. *Archiv f. Psychiatrie und Zeitschrift f. Neurologie, 181:* 537–546, 1952.
26. Steinwachs and Barmeyer: Beziehungen der Micromotorik zu den Reifungsgraden in der Pubertaet. *Zeitschr. f. menschl. Vererb. u. Konstitutionslehre, 31:* 174–192, 1952.
27. Thewlis, M. W., and Swezy, I. C.: *Handwriting and the Emotions.* New York: American Graphological Society, 1954.
28. Victor, F.: *Handwriting: A Personality Projection.* Springfield, Ill.: C. C Thomas, 1952.
29. Wolff, W.: *Expression of Personality: Experimental Depth Psychology.* New York: Harper and Bros., 1949.
30. Wolff, W.: *Diagrams of the Unconscious.* New York: Grune & Stratton, 1949.

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ACUTE EPILEPTIC DEMENTIA

A Contribution to the Problem of Mental Deterioration in Epileptics

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Acute epileptic dementia is an apparently little recognized syndrome.

Epileptics commonly suffer slow deterioration of intelligence. For example, among 536 cases outside institutions and normal at birth, Lennox (7) found a severe loss of faculties in only 6% of those with less than a year's history, whereas after 15 years of fits the figure had risen steadily to 20%.

Without other definite cause, such brain damage might be attributed to the convulsions, but this has always been strongly contested since many epileptics do not become demented and even attain intellectual eminence. Therefore authorities often ascribe this gradual dementia to the same unknown process that also is responsible for the fits, or alternatively, to prolonged medication, invalidism, and institutional life (6).

A clinical entity is reported here which may be relevant to the problem and which renders doubtful the belief that convulsions are necessarily harmless to the brain. Three instances are described where a catastrophic series of fits resulted in profound and lasting dementia: two in children with pre-existing epilepsy and one in a backward child, probably epileptic too. Further, some details will be presented of six similar cases that indicate the condition may be confused, perhaps commonly, with virus encephalitis. An experience which seems comparable will be quoted from ECT, and the cause of brain damage during convulsions considered.

Case 1: This child was normal in health and development apart from occasional epileptic fits. Following convulsions lasting some hours, he was left a complete idiot, and in this state 15 months later, aged 5 years and 4 months, he was admitted to the Fountain Hospital.

Family history. The father was a lifelong epileptic, 26 at the child's birth. Although he had been under statutory supervision as a mental defective and had a poor employment record, he could read and write quite well and seemed to be of dull normal intelligence. Judged clinically and from medical reports, he was probably a case of personality disorder with idiopathic epilepsy that nowadays would have been treated as a child guidance problem rather than as a mental defective.

The mother, seven years younger, had a superior style of dress and speech which contrasted strangely with her juvenile husband and his obvious slum background and with her own work as a cinema usherette. She came from a broken home and gave birth to the child before her husband's mother would consent to the marriage.

The siblings were a twin brother, who died at the age of 16 months of non-specific gastroenteritis in St. Thomas's Hospital, and who was apparently normal; and a younger premature baby who died shortly after birth.

Personal history. Pregnancy was uneventful. Labor was six weeks before the expected date, and the hospital reported that the patient was the first-born twin and a breech delivery. He weighed 3 lb., 11 oz., and his condition and progress were good.

Infancy and early childhood were normal; he was breast fed for 4 months, took to solids easily, and could walk at about one year. Later he talked and acquired sphincter control at the ordinary times; he could sing songs, ride a tricycle, and appeared to be growing up like any other child. He began to have fits at 2½ years, but no associated defect of development was found at either of the two hospitals he attended for this.

History of illness. At 2½ years, after attending a hospital for 4 days with acute otitis media, he was admitted after having two convulsions. He had once before had a fit. He was discharged 9 days later, taking ⅛ grain of phenobarbitone twice daily.

At 3 years, he attended another hospital because of fits, having had about six more coinciding with sore throats, in the interim. The dose of phenobarbitone was doubled, and he kept well under out-patient care.

One morning 9 months later, having awakened hot and fretful, he started to convulse, and 2 hours later, still convulsing, he was urgently re-admitted to hospital. The tonsils were large and inflamed, and he was incontinent, but there were no other physical signs then or in the ensuing few days, aside from some doubtful and varying inequality of muscle tone. Despite anti-convulsant drugs, the convulsions persisted for another 3 hours or more, and convulsive movements recurred on the fourth day. For 6 days he could not be roused, nor could he take fluids by mouth.

X-rays of skull and chest, WBC count, urine examination, WR and Kahn were all negative. The CSF was examined after 48 hours, 4 days, and 7 days and was quite normal but for some excess globulin in the second specimen. An EEG on the sixth day showed large delta potentials at 1–2 per second in all areas, perhaps greater posteriorly and on the right, without other significant activity; and except for less bilateral asymmetry, it was unchanged when repeated 9 weeks later under thiopentone. Epilepsy was the likeliest cause.

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After 6 days some responsiveness returned, and he appeared to look at things. Subsequently, he could be fed but he remained restless. After 18 days he could sit upright, but aimless disturbance persisted. He would lick the pillows and bite his clothes, and neither speech nor recognition of his parents ever returned.

Tone in the upper limbs varied, at times seeming increased on the right, at others diminished, but, ultimately, there was thought to be a tendency to left-handedness. Otherwise, there were no abnormal neurological signs.

At the end of 4 months fits returned, chiefly minor attacks, but several convulsions coincided with a sore throat. He remained restless and disorganized, unable to feed himself, unsteady on his feet. Finally, he caught mumps and entered a fever hospital.

On admission to the Fountain Hospital, aged 5 years and 4 months, his behavioral level was only that of a six-month-old infant. He needed spoon feeding, could only crawl about, and was poorly responsive apart from being inclined to chew whatever was in reach.

Physical examination was quite negative. He weighed 42 lb.; the head circumference was 20 inches; and X-rays of skull and chest, the blood WR, and tests for phenylketonuria were all normal.

During 2½ years observation he has changed little. He can now totter about and respond to his name. There still is no sphincter control, and convulsions and frequent petits mals continue.

Dementia would appear irreversible.

Case 2: Until the aged of 3½ years, this child was normal, or even advanced in mental growth, and in good health apart from epileptic fits twice and a symptomless congenital cardiac anomaly. Following a series of convulsions which lasted some hours she was left completely demented, and 6 months later she was admitted, aged 4 years, to the Fountain Hospital.

Family history. The parents and brother were of superior intelligence and were extremely tall, while the mother and brother had large skulls with overhanging foreheads. The mother's head was 25 inches in circumference and the brother's was 22 inches at 5 years. These points are mentioned to emphasize the familial tendency to tallness and to this type of large skull. The latter had once led, in the patient's case, to a diagnosis of hydrocephalus.

There were no illnesses or other relevant details.

Personal history. Pregnancy and labor were uneventful, at home; the birth weight was 7 lb., 2 oz.

Infancy was normal with 9 months of breast-feeding. At 2 months, when she attended a children's hospital for conjunctivitis, it was noticed that her head was large and that there was a cardiac murmur suggestive of ventricular septal defect.

In early childhood she sprang up well, becoming tall for her age, forward with speech, nursery rhymes, and jigsaw puzzles.

History of illness. At 2 years and 2 months, she was investigated at the same hospital following a convulsion; hydrocephalus was suspected, and there was an abnormal EEG with many fast rhythms. However, she continued to progress normally. A year later she was attended after another fit.

At 3½ years she was urgently re-admitted in status epilepticus which had begun without warning. In fact, she had been perfectly well only 36 hours earlier when she was seen for a bruise on her forehead. Despite sedation, convulsions continued for a further 3 hours and unconsciousness for 2 days; subsequently she was clouded. Though for a few days there were, possibly, signs that she recognized her parents, she never regained the ability to speak, walk or feed herself, or to perform any coordinated purposive activity.

After a week she was transferred for neurosurgical investigation which proved negative; skull X-rays, ventriculography, and CSF were all normal. Later on, there was a transient tendency to choreo-athetoid movements, but no abnormal neurological signs occurred otherwise.

On admission to the Fountain Hospital, aged 4 years and 1 month, she presented an infantile level of organization with patchy residues of previously-acquired behavior patterns. Thus she had an intelligent, watchful face and responded pleasurably to her parents, smiling and gazing from one to the other, listening to certain nursery rhymes and ignoring others. Otherwise, her reactions were very limited; she lay sucking her thumbs, unable to sit upright, without sphincter control, shrieking monotonously at the mildest disturbance, but she could drink from a cup if it was held for her. Her developmental age on the Vineland Scale was only 4 months.

Physical examination was largely negative. She was 43 inches tall; the head was 21 inches in circumference, resembling her mother's and brother's, with a slightly overhanging forehead and a large occipito-frontal diameter of 7½ inches; skull X-ray revealed two burr holes and remnants of lipiodol in the cisterna magna. The neurological findings were mild, generalized hypotonia, reduced tendon and absent abdominal reflexes, but no other abnormalities. There were apical and basal cardiac thrills with a loud, blowing murmur over the whole precordium. Blood WR and phenylketonuria tests were negative.

During 15 months of observation there has been little change; she is still hypotonic but can now sit upright. Otherwise there is no improvement.

Case 3: This child had always been backward and disturbed. She was admitted to the Fountain Hospital at 4 years, 4 months with a history of complete dementia following status epilepticus 11 months previously. Since then she has never been free of convulsions although there was none prior to this event. However, she had been taking bromide for the preceding 18 months for suspected minor epilepsy, and her father was epileptic.

Family history. The father had attended a neurological hospital since childhood with idiopathic epilepsy. He was a shop assistant.

The mother and two younger siblings were in good health.

A maternal cousin had entered a mental deficiency hospital at 14 and was reported to be feeble-minded with emotional explosions.

Personal history. Pregnancy and labor were reported by the hospital to have been uneventful. The neonatal condition was good, the birth weight 8 lb., 5 oz., and she was breast fed for 6 weeks. Her infancy at first showed nothing amiss; she sat up at 8 months and stood at 1 year, but she could not really walk until 2 years. She was still unsteady on her feet when 3½ years old.

By 3½ years, though still without sphincter control, she could feed herself messily, manage a cup with supervision, understand and use simple speech, and join in songs.

History of Illness. During her second year it became obvious that the child was abnormal. She had bouts of screaming that might go on for hours, she would eat dust, dirt, feces, and was given to banging her head against the wall. Also she had brief fits of vacancy, suspected to be petit mal attacks. At 20 months, she was put on phenobarbitone. Eventually, bromide was substituted at another childrens' hospital where a diagnosis was made of moderate mental defect with cause unknown.

Eighteen months later, at 3½ years, she was admitted to a hospital, having been found that morning in bed unconscious and convulsing. There were no premonitory symptoms. Despite sedation convulsive activity continued for a further 2½ hours, and she continued, with periodic twitching, stuporose over the next 2 days, but able to drink. CSF, skull X-rays, and urine were all normal; the WBC count was 27,400.

She was transferred for neurosurgical investigation on the third day as stupor seemed deepening. There was now some weakness in the right lower facial musculature, absence of the right abdominal reflexes, and moderately increased tone and tendon reflexes, without loss of power, in the right limbs. An EEG on the fifth day gave continuous ½–2 per second 75 μv. activity, while at the end of the record, there appeared repeated epileptic discharges at intervals of 1½ to 2 seconds, consisting of 1 per second sinusoidal waves with or without 1 to 2 spikes. Such complexes were considered to resemble those of subacute inclusion body encephalitis, though not to be peculiar to it. Next day the CSF was re-examined, and a borderline pleocytosis of 12 cells was found. However, on the tenth day the EEG was repeated and merely gave a tracing to be found in any comatose patient, with regular ½ to 3 per second high voltage activity in all areas. On the eleventh day the CSF was normal.

On the twelfth day a ventriculogram was performed and found to be normal.

By the end of another month, there was some regain of consciousness, and she could usually take food; the weakness in the right side of the face was now doubtful, and the only abnormality of tone was symmetrical increase in the lower limbs. She returned to the hospital and remained there for 9 months, inert, poorly accessible, very difficult to feed so that tube feeding was sometimes necessary. The tone in the legs decreased, and ability to raise the head returned over 8 weeks. One more convulsion occurred.

On admission to the Fountain Hospital, aged 4 years and 4 months, she displayed the primitive responses of a small baby. She lay silent and passive, with no spontaneous activity except side to side head rolling; eye movements were conjugate, but she would only follow light or an object momentarily, and her reaction to pain or loud noise was seldom more than a tightening of the face and increased head rolling.

Physical examination added little. Her weight was 33 lb., height 40 inches, head circumference 19¼ inches with skull X-ray normal apart from burr holes, chest X-ray and tests for phenylketonuria negative. There was marked vasomotor instability with dermographia; the tendon reflexes were reduced, the abdominal reflexes absent, and there was a tendency to extensor plantars and to an athetoid quality in movement of the upper limbs.

During a year's observation, the dementia seems irreversible. She still cannot chew solid food or sit up, and she lies about vacantly all day. Convulsions have continued, occurring every few days at first, but about once a month with phenobarbitone since.

THE TERM "ACUTE EPILEPTIC DEMENTIA"

Cases of this kind though uncommon are not very rare: these three were observed among some 180 admissions over a 2-year period at a hospital for mentally-retarded children. However, so rooted is the opinion that convulsions do no serious damage to the brain that alternative explanations for such cases are always sought intensively. "Encephalitis" is the most frequently invoked, but vascular accidents and degenerative diseases are often considered. In my opinion, it may be shown that these diagnoses have very little to recommend them, while more convincing suggestions can be made to explain how convulsions might bring about such brain damage.

Alternative diagnoses and their exclusion

1. *Encephalitis.* Pre-existing cerebral pathology can be presumed in all these cases. Cases 1 and 2 were known epileptics and in neither was the onset of the prolonged fits attended by any novel circumstance that differed from previous fits. Case 3 was a known mental defective with an epileptic parent, and who with suspected petit mal had already taken bromide for 18 months before the acute illness and who continued to have fits after it. Only in case 1, a child previously particularly prone to convulsions whenever febrile, were there any prodro-

TABLE 1.—THE DOUBTFUL CASES AMONG 9 THAT ARE ASCRIBED TO VIRUS ENCEPHALITIS AMONG 600 MENTALLY-DEFECTIVE CHILDREN

No.	Clinical Details	Comment
1	Normal development until sudden onset of status epilepticus at 1 year, with survival as an epileptic idiot. Urgently admitted to hospital, and over 5 months failed to improve: no fever nor neurological signs nor other evidence of encephalitis.	A convulsive episode with permanent sequelae.
2	Normal development until 2¼ years. Admitted to hospital 2½ hours after sudden onset of convulsions, still twitching, febrile a few hours (? while convulsing), needing tube feeding over a period, with frequent prolonged convulsions recurring; C. S. F. normal, no neurological signs: survived as an epileptic idiot.	Ditto
3	Normal development until 2½ years. Sudden onset coincidentally of status epilepticus and chicken pox: convulsed for 18 hours, comatose 3 days, stuporose 1 week or more: afebrile with normal C. S. F. throughout: brain biopsy not indicative of encephalitis. Survived an imbecile with slight hyper-tonus and athetoid tendency in R. upper limb.	Ditto Brain biopsy is referred to in the text.
4	Normal development until 2½ years. After 2 days of fretfulness and rigors, had sudden onset of repeated convulsions with intervening coma, persisting 10 days. Survived an idiot with slight hemiparesis.	A convulsive episode with permanent sequelae in a febrile child. Compatible with encephalitis but no conclusive evidence.
5	Normal development until 13 months but had had febrile convulsions. Sudden onset of status epilepticus and coma for 2 days while recovering from suspected whooping cough and survived an idiot with slight hemiparesis.	Ditto with previous history of febrile convulsions.

mal symptoms, and these amounted in all to 3 or 4 hours' malaise. Apart from profound dementia and convulsions, neurological abnormalities were slight and transient in all.

The diagnosis of supervening encephalitis, therefore, has no positive evidence to support it unless in case 3 the borderline pleocytosis in one of the CSF examinations and the passing abnormality of the EEG can be accepted as such. Actually, such a diagnosis would never arise were it not for a lack of other possibilities and a reluctance to believe that convulsions alone can cause acute and gross brain damage. Possibly similar examples to these are included in that clinical category of encephalitis presented as sudden and prolonged convulsions and coma, which Brewis (1) distinguished among a series of 93 cases in childhood. The tendency to ascribe these cases to some virus encephalitis is illustrated in table 1. This table reveals that of the nine attributed to encephalitis among 600 mentally-defective children at the Fountain Hospital, six are remarkably like the cases here, with no decisive evidence for encephalitis. The only difference is that five had no history of epilepsy before the disastrous convulsive episode.

2. *Cerebral vascular accident.* A rupture or an occlusion of cerebral blood vessels might be postulated in these cases. Against this is the impossibility of conceiving a vascular lesion massive enough to cause profound and persistent dementia, presumably by wide-spread injury to the cerebral cortex, yet producing no bleeding into the CSF nor any major or lasting signs in the CNS otherwise. Damage to the cortex is prominent with thrombosis of the superior sagittal venous sinus, but this occurs only as a hazard of babies with some severely dehydrating illness and does not appear relevant to the pattern of these children.

Bridge (2) has observed permanent paralysis and mental change to follow a succession of fits in epileptics who had little or no signs previously of brain damage, and he considers this to represent a vascular accident rather than ordinary status epilepticus. The cases here are different in that no permanent paralysis or focal signs developed. In this respect they also differ from the syndrome of vascular occlusion in healthy children of which Ford (3) records 50 cases with hemiplegia of sudden onset accompanied by fits and with dementia ensuing, a condition at one time called "Marie-Strumpell encephalitis".

3. *Degenerative brain diseases*. The remaining possibility is that these children were the victims of some undiagnosed degenerative process of which their epilepsy was merely a symptom. This seems scarcely tenable as two were quite normal beforehand in mental development and general health. The third, if backward, was certainly showing mental development and not deteriorating. Furthermore, since the destructive episode, there is no hint of continuing neurological degeneration, and, in fact, cases 1 and 2 have had slight regain of function.

How may convulsions produce dementia?

Epilepsy is said to be the commonest cause of dementia in childhood (3) and Bridge (2) indicates that the severity of any dementia runs parallel to the frequency, duration and intensity of convulsions. Also supporting the view that convulsions themselves injure the brain, there is the fact on which Spielmeyer (10) laid emphasis: that certain cerebral lesions such as sclerosis and loss of neurons in the hippocampus, the cerebellar Purkinje cell layer, and the occipital cortex, all of which have long been recognized in epileptics, are probably the result of convulsions as they occur regularly with them, irrespective of causes so diverse, for example, as tumor, head injury, or eclampsia. Scholz (9) considers convulsions in early childhood to be especially damaging and capable of massive cerebral destruction.

It is well-known that convulsions may be followed by transient phenomena indicating severe cerebral impairment. Temporary dementia lasting some weeks followed status epilepticus in three infants observed by Ford (3). Temporary dementia is a common sequel of regular therapeutic convulsions, whether induced chemically or electrically. Though it may be manifest only as a mild defect of memory over a few weeks, occasionally serious mental disorganization is produced. Such effects are related in their severity to the number and spacing of treatments, but this is no more a constant rule than with spontaneous fits. Rare though it is, extremely exaggerated and enduring dementia can result from convulsion therapy, and the following example from my experience illustrates this:

> *Case 4:* A woman of 34, with a schizophrenic breakdown, was given 8 E.C.T's in the course of 3 weeks, and a florid Korsakow psychosis appeared. For months she could not retain new memory impressions from one hour to the next, and she would confabulate a fresh identity for me whenever I greeted her, affecting to recognize me as anything from an R.S.P.C.A. collector to an election official. Eventually her time sense improved, and the tendency to confabulation faded, but her memory never recovered fully, and she was left moderately demented while the old paranoid ideas re-emerged.

Abrupt and extreme dementia, with no lasting signs of damage in the nervous system elsewhere, is a characteristic sequel of acute cerebral anoxia. If the four examples of such dementia quoted here can be explained by an episode of this sort, then perhaps the insidious intellectual decline to which epileptics are prone is the result of cumulative damage by a similar process supervening repeatedly in milder form with convulsions.

The evidence for cerebral anoxia with convulsions

1. *Asphyxia*. Obvious asphyxia is a feature of convulsions. Respiration is interrupted for the duration of the fit, and subsequently it may further be seriously obstructed by salivary and bronchial secretions. Cyanosis is usual and often extremely intense, and when fits occur in succession, it may be alarmingly prolonged. Bridge (2) points out that petit mal seizures do not seem to cause any injury comparable with convulsions, and he emphasizes the injurious role of anoxia in the latter.

2. *Cerebral vascular spasm*. Neurosurgery has revealed that convulsions are associated with altered tone in the cerebral blood vessels which may last for hours. Any such angiospasm must aggravate locally the oxygen deficit set up by insufficient aeration of the blood.

3. *Experimental and pathological findings*. The cerebral lesions with convulsive states, to which reference has been made, were attributed by Spielmeyer to ischemic necrosis resulting from localized vascular disturbances. Gildea and Cobb (4) showed that they could be reproduced in cats by cerebral ischemia. Acute lesions are described by Zimmerman (11) in children dying during prolonged convulsions. These include cerebral vascular congestion,

capillary stasis with diffuse petechiae, and foci of degenerating neurons that are conspicuous in those cortical areas that tend to show atrophy and gliosis in subjects with long-standing epilepsy. As he found exactly similar changes in children who died of respiratory failure due to pneumonia or asphyxia, he concluded that anoxia is the injurious factor common to these and to convulsions. Scholz (9) in his account also attributes the lesions associated with severe fits to ischemic and anoxic damage. A cerebral biopsy early in the illness of case 3 in the table has since come to light, and it describes massive neuronal atrophy in all the cortical layers, quite unlike encephalitis, and suggestive only of some sudden destructive episode such as anoxia.

The cerebral lesions recorded with experimental and clinical conditions of anoxia and ischemia are fully reviewed by Hoff *et al.* (5). From this it seems clear that neuronal atrophy and gliosis, distributed as in epileptics, accompany chronic anoxia, and that acute anoxia produces a picture such as when death follows prolonged fits, with circulatory disturbance, congestion, small hemorrhages, and neuronal damage which is severest in certain cortical areas.

Conclusions. Since all nerve cells, particularly those of the cortex, are very susceptible to oxygen lack, and since functional mechanisms that bring about cerebral anoxia are conspicuous during convulsions, it seems reasonable 1) to accept that the gradual dementia sometimes accompanying chronic epilepsy may be caused by recurrent and cumulative anoxic injury during convulsions, and 2) to suggest that sudden and total dementia may follow the occasional disastrously prolonged convulsive episode. The cases described here are advanced as examples of such a syndrome of "acute epileptic dementia". A very similar case has recently been recorded by Meyer *et al.* (8).

SUMMARY

The mental faculties of epileptics often steadily decline; the cause for this is uncertain.

Here three cases are described in which sudden and lasting dementia followed a calamitous series of convulsions. Two were previously known epileptics, while the third child was backward, probably with minor fits, previously taking bromide, and with an epileptic father.

Reasons are submitted for excluding other diagnoses, for ascribing the brain damage to the convulsive episode preceding it, and for questioning the opinion that convulsions, in themselves, do no injury to the brain. Other evidence for such damage is quoted, and a related misfortune with ECT is outlined.

The noxious influence of convulsions is attributed to cerebral anoxia; the means by which they bring this about are discussed.

It is concluded that dementia in epilepsy may be the result of repeated mild injury, probably anoxic, that occurs with fits, and that the cases here exemplify an occasional similar but massive injury, a syndrome of "acute epileptic dementia". It is probably not very rare, and in fact, as illustrated, it is perhaps commonly confused with virus encephalitis as a cause of mental defect.

I am very grateful to the following physicians for full information about these patients while in their care and for generous permission to quote it: Dr. J. D. Burkinshaw, St. James Hospital, Balham; Dr. N. O. Richards, Westminster Children's Hospital; Dr. Mary J. Wilmers, Belgrave Hospital for Children.

I thank Dr. Chloë Majolier for most helpful criticism.

BIBLIOGRAPHY

1. Brewis, E. G.: Recent Experience of Encephalitis in Childhood.
2. Bridge, E. M.: *Epilepsy and Convulsive Disorders in Children.* New York: McGraw Hill, 1949.
3. Ford, F.: *Diseases of the Nervous System in Infancy, Childhood, and Adolescence.* Springfield: Thomas, 1945.
4. Gildea, E. F., and Cobb, S.: Effect of Anemia on the Cerebral Cortex of Cats. *Arch. Neurol. & Psychiat., 23:* 876, 1930.
5. Hoff, E. C., Grenell, R. G., and Fulton, J. F.: Histopathology of the CNS after Exposure to High Methods, Hypoglycemia, and other Conditions Associated with Central Anoxia. *Medicine, 24:* 161, 1945.
6. Kinnier Wilson, S. A.: *Neurology*, Ed. Bruce, N., Arnold, 1940.
7. Lennox, W. G.: Personal communication quoted by Bridge (loc. cit. p. 487), 1949.
8. Meyer, A., Beck, E., and Shepherd, M.: Unusually Severe Lesions in the Brain Following Status Epilepticus. *J. Neurol., Neurosurg. & Psychiat., 18:* 24, 1955.
9. Scholz, W.: *Die Krampfschadigungen des Gehirns.* Berlin: Springer, 1951.
10. Spielmeyer, W.: Anatomic Substratum of Convulsive States. *Arch. Neurol. & Psychiat., 23:* 869, 1930.
11. Zimmerman, H. M.: The Histopathology of Convulsive Disorders of Childhood. *J. Pediat., 13:* 859, 1938.

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FURTHER NEUROLOGICAL STUDIES WITH PIROMEN

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Somewhat more than one year ago, my first paper on "The Action of Piromen on Certain Neuropathologic States" appeared in print (4). More valid conclusions can now be drawn since there has been a longer period for observation in the cases formerly described and because there have been additional cases.

Piromen is described by the manufacturers[1] as a sterile, non-protein and non-anaphylactogenic bacterial component whose active factor appears to be a complex polysaccharide.

The work of Stuart, Clement, Windle, Scott and their co-workers (1, 2, 5–10) showed that:

1) Piromen inhibits glial scar formation and permits neuronal growth across the acutely transected spinal cord.

2) It enhances antibody formation and stimulates activity of lymphatic organs.

3) After prolonged administration extramedullary hemophoesis in the liver and spleen of rabbits and cats was noted.

4) Adrenal gland and hypophysis show a definite relation to the action of Piromen. This is shown by the alteration of granulocystosis after adrenalectomy or hypophysectomy.

5) Evidence of the action of Piromen on endocrine glands has been demonstrated histologically.

6) Electrophysiologic studies demonstrated conduction in lateral columns of spinal cord across the site of transection after treatment with Piromen.

7) The site of transection of the spinal cord must show less than 1 mm. of separation in order for healing to take place with Piromen.

8) The bacterial polysaccharide caused no regeneration in animals which were treated for less than eight days.

Since these observations were of clinical significance, I tried the Piromen on four groups of cases:

Groups 1 and 2. Injury of the spinal cord without visible damage and laminectomy for partial compression of spinal cord.

Case 1: J. M.—Male, age 18 years, quadriplegia, following car accident. He improved with Piromen and had stronger arm movements, return of upper abdominal reflexes, improvement in sensory level including slight return of bladder and rectal sensation and slight return of finger movements. These changes occurred within five months. However, the boy died of sunstroke while on vacation down South.

Case 2: F. R.—A 22-year-old male suffered paralysis of both lower limbs as a result of an automobile accident. He showed x-ray evidence of a fracture dislocation of the first lumbar vertebra and had a complete flaccid paralysis as a result. Bladder and rectal control were present. The patient did not improve for two weeks following laminectomy. However, after the tenth injection he began to move his toes. This patient walked out of the hospital within three months of starting his Piromen injections. He has remained well and has never returned for further treatment.

New Case 3: R. F., age 18 years, male, white, suffered a quadriplegia from a fracture dislocation at C5-C6. He was in a university hospital where cervical traction was tried without any apparent improvement. Five months after the accident, the boy was transferred to another hospital where a spicule of bone and a herniated disc were removed from compressing the spinal cord. The cord was congested, but no obvious disruption could be seen. The patient was put on Piromen injections about two weeks after the decompression of the spinal cord; within this time there had been no improvement. Within two weeks (6 injections), the boy began moving his fingers. After injections for 3 months, he could pick up a glass of milk. Within five months, he could sit up in a wheel chair for hours and could feed himself. He was then transferred to a University Rehabilitation Centre where he is being taught to stand.

New Case 4: Mr. L., a colored male, middle-aged, 47 years, suffered a left hemiplegia and right hemiparesis following a fracture dislocation at C5-C6 which occurred after an automobile accident. Cervical traction was tried for two weeks but with no apparent improvement in motor power or in ability to pass urine. Thereafter, the patient was put on Piromen injections. After two weeks of injections (6 injections) he began to improve in motor power in all four limbs, and micturition was carried out without difficulty. Within one month of starting the injections, Mr. L. was walking about the ward. There was some residual weakness in the right limbs at the time of discharge from hospital.

Case 5 (formerly case 1—group 2): R. P.—Lives a normal life with little neurological residual.

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[1] Piromen has been donated for this study by the Travenol Laboratories.

Case 6 (formerly case 2—group 2): M. V. has never returned for further follow-up.

Case 7 (formerly case 3—group 2): A. F.—This patient showed temporary improvement with Piromen but has shown no further progress.

Case 8 (formerly case 4—group 2)—Dr. Criscione's case—Mrs. C: She has shown steady improvement in the motor power of her lower limbs following the institution of Piromen injections. This patient was paraplegic following the removal of a spinal cord tumor in 1946.

New Case 9: M. S.—Female, colored, age 57 years. Showed acute paraplegia. Diagnosis of mediastinal tuberculous abscess was made by x-ray and later confirmed by biopsy at another hospital. Laminectomy with a course of Piromen caused temporary improvement in motor power and urinary control. However, this soon retrogressed, and she has never responded to further injections of Piromen.

New Case 10: J. H.—Male, age 44 years, had 2 courses of radiation therapy following laminectomy for hemangioma at D12-L1. He has urinary control but has been paralyzed in both lower limbs for a number of months. He began to get some return of motor power within six weeks of starting Piromen injections. The patient has not returned for follow-up.

New Case 11: A. S.—Male, white, age 54 years, became paralyzed in both lower limbs within two weeks of getting a sudden back pain after pushing a car. Myelogram showed a partial block to pantopaque from D10-D12. Laminectomy decompressed the cord, and the herniated discs were removed. The cord was cyanotic and non-pulsating until it was completely decompressed. There was no improvement for about one week following laminectomy. Piromen injections were instituted, and the patient improved in motor power and in urinary control, but not markedly. Six months later, his spine was re-x-rayed, and a generalized decalcification was seen with compressions of many of the bodies of the vertebrae.

New Case 12: C. R.—Female, white, age 47 years, diagnosed as Multiple Sclerosis at a university hospital. Suffered from paraperesis with paresthesia in upper limbs. Walked with an ataxic gait, showed bilateral positive Babinski reactions and had hyperactive deep reflexes in all limbs. There was no scanning speech nor nystagmus. Laminectomy revealed a herniated cervical disc at C5-C6. Following laminectomy, the patient became quadriplegic. Piromen injections were instituted. There has been slow but gradual improvement in motor power in all limbs. This has taken about 18 months, and she is not yet as "good" as she was before surgery.

Case 13: B. N.—Female, white, age 40 years, had laminectomy for upper thoracic cord neoplasm in Nov., 1951. There was improvement in motor power after operation, but patient could not walk nor stand without help. About 1½ years after operation (1953), Piromen injections were started. She has improved steadily, so that she can now walk up and down stairs by holding on to the bannister.

New Case 14: E. S.—Female, white, nearly middle age, developed paresis and paresthesia in both upper limbs following cervical laminectomy for herniated cervical intervertebral disc at C5-C6. There was no improvement in motor power for about one week when Piromen injections were instituted. There was steady improvement thereafter so that within four months the patient could type letters. However, she is not completely cured and is still getting some physiotherapy.

New Case 15: D. E.—Male, white, age 48 years, complained of difficulty in swallowing and attacks of choking. The patient showed positive Babinski reaction on the right, positive Hoffman sign, bilaterally, absent abdominal reflexes and absent gag reflex. Except for wasting of right suprascapular muscle, there was no other muscle wasting. Laminectomy with removal of herniated disc at C4 and Piromen injections caused return of gag reflex and feeling of well being. However, the patient died in a veteran's hospital one year later; the diagnosis was amyatrophic lateral sclerosis.

Group 3. Laminectomy in cases showing the Multiple Sclerosis syndrome.

No further cases beside the original six reported previously have been added to this group.

There has been no additional progress in these six cases, and they have stopped using Piromen.

Group 4. Cases diagnosed as Multiple Sclerosis and never disproved by surgery. Six cases were originally described. The Piromen injections were tried on five additional cases, making 11 cases in all. Of these 11 cases, eight showed some improvement both subjectively and objectively, but results were not remarkable.

Case 3 (Group 4): B. F., is still teaching and carries on well. She will have a return of all her Multiple Sclerosis signs and symptoms when she eats chocolate, but these will disappear within two weeks (6 injections) of instituting the Piromen injections.

SUMMARY AND CONCLUSIONS

Piromen seems to have definite value in the cases that have undergone surgery because of spinal trauma, where there has been no obvious disruption of the spinal cord.

There seems to be some improvement with Piromen in cases where surgery was performed for compression of the spinal cord. There will not be any return of function in fibers that have been physiologically destroyed. This applies also to the spinal cords of patients who have the signs and symptoms of Multiple Sclerosis caused by a high, cervical, compressive lesion.

Piromen injections in the patients who have the Multiple Sclerosis syndrome are only of moderate beneficial effect. Usually in most cases that are losing, or have lost, ambulation, Piromen injections have some slight beneficial effect.

No patient has been made worse while undergoing treatment with Piromen. All in all, Piromen has a definite place in the treatment of certain neurological conditions.

Piromen has given the best results when administered in doses of 5 gamma strength. During the first week Piromen can be given daily, either subcutaneously or intravenously. Then it is to be administered every second day by subcutaneous route. A two-week rest from injections is taken after each 10 cc. ampule is finished. One vitamin B1, 25 mg. tablet and one vitamin B12, 25 mg. tablet are taken three times daily. Physiotherapy is of great help in speeding up the process of improvement.

BIBLIOGRAPHY

1. Clemente, C. D., *et al.*: Regeneration of the transected spinal cord of adult cats. *Anat. Rec., 109:* 280, 1951.
2. Clemente, C. D., Chambers, W. W., and Windle, W. F.: Blending of regenerating peripheral fibers with cerebral cortex through glial barrier inhibition. *Am. J. Physiol., 167:* 774, 1951.
4. Rosner, S.: The action of Piromen on certain neuropathologic states. *J. Nerv. & Ment. Dis., 120:* 22, 1954.
5. Scott, D., Jr., and Clemente, C. D.: Conduction of nerve impulses in regenerated fibers of the spinal cord of the cat. *Am. J. Physiol., 167:* 825, 1951.
6. Scott, D., Jr., and Clemente, C. D.: Conduction of nerve impulses in the regenerated fibers of the spinal cord of the cat. *Arch. Neurol. & Psychiat., 67:* 830, 1952.
7. Scott, D., Jr., and Clemente, C. D.: Mechanism of spinal cord regeneration in the cat. *Fed. Proc., 11:* 143, 1952.
8. Stuart, E. G.: Possible mechanisms of action of the bacterial polysaccharide complex, Piromen. Read before the American Physiological Society Meetings in New Orleans, Sept. 4–6, 1952.
9. Windle, W. F., *et al.*: Structural and functional regeneration in the central nervous system. *Arch. Neurol. & Psychiat., 67:* 553, 1952.
10. Windle, W. F., and Chambers, W. W.: Spinal cord regeneration associated with a cellular reaction induced by administration of a purified bacterial pyrogen. Internat. Anatomical Congress Abst. July 24–28, 1950, p. 196, Oxford, England.

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BOOK NOTES AND REVIEWS

Books received are acknowledged and given a brief description in this section. Selections serving a variety of interests will be made from these for a more extensive review, as far as space will allow.

BOOK NOTES

Glees, Paul: NEUROGLIA, MORPHOLOGY AND FUNCTION. [Springfield, Ill.: Charles C Thomas (#260 American Lecture Series) Pp. 111—44 Illustrations 1955. $5.00.]

This brief monograph is concerned with the glial tissue in man and animals. It is primarily a review of the literature that has accrued since the introduction of silver stains brought the study of neurologia into a prominent place in neuropathology. This critical survey of what has been published and known about the various forms of neuroglia could well serve as a foundation for advanced studies that should be coming along in the physiology and biochemistry of the brain. Histochemistry has still to have its day as a major contributor to neurological and psychiatric medicine.

It will serve as a handy outline for orientation in the historical background, comparative studies, morphology and histogenesis of this system of tissues for all workers and students interested in brain tissue. There are 44 figures, many of which are drawings and about 300 references to the literature. Instructors in anatomy and neurology will find it particularly helpful.

Sheldon, W. H.: ATLAS OF MEN: A GUIDE AND HANDBOOK ON SOMATOTYPING THE ADULT MALE AT ALL AGES. [New York: Harper and Brothers: Pp. xvi + 357. Illustrated. 1954. $10.00.]

Most psychiatrists who have any interest at all in constitutional factors in personality and temperament are acquainted with Sheldon's works since these are quoted extensively in psychiatric literature.

This large beautifully printed and illustrated book is the fourth volume of the Human Constitution series based on the author's system of somatotyping and describing human physique. Here one finds multiple examples of each somatotype at various ages. The material is presented in two parts.

Part I discusses the theory and various factors such as the influence of age, sex, nutrition on the somatotype and individual differences within it. Part II, the greater portion of the book, is devoted to photographs of 1,175 adult male physiques with detailed definitions, weight curves, and impressions of psychological components.

The method of study followed is important and may do something to clarify the controversies regarding constitutional types and their validity in the clinical field. It is obvious, however, that additional study, testing, documentation and critical analyses will be necessary before all of the material can be accepted for scientific uses. The excellent illustrations insure a permanent value to the book, but the interpretation of what they mean in medicine and psychology may change from time to time as methods of investigation are improved or modified to include additional features, some of which are undoubtedly inside the skin and in the bodily cavities. The book as a whole is very stimulating and thought provoking.

ANNUAL REPORT OF THE SMITHSONIAN INSTITUTION 1953. [Washington, D. C.: United States Printing Office: Pp. 418. Illustrated. 83 plates. 1954.]

Many scientists representing widely different disciplines look forward with keen anticipation to the appearance of these yearly reports on the activities of the staff at the Smithsonian Institution. Among many other items of interest, the physician should read the article on "Science, Art and Education" by R. E. Gibson who deals with fundamental relationships between various aspects of these functions.

Other articles that should catch the doctor's eye are "Radioisotopes" by Paul C. Albersold who describes their uses in medical research, diagnosis, therapy, etc.; "Genetics and the World Today" by Curt Stern: a review of the present situation and the outlook; and "Climate and Race" by Carleton Coon.

The numerous illustrations throughout the book are excellent. The text is extremely interesting and will enrich any library.

BOOK REVIEWS

Bleuler, M.: ENDOKRINOLOGISCHE PSYCHIATRIE [Stuttgart: Georg Thieme Verlag: Pp. 498, with 30 illustrations. 1954. D.M. 46.50.]

It is probable that all of the tissues of the body are affected in specific ways by the secretions of the endocrine glands, and there are several nervous and mental disorders that present pathological endocrine conditions prominently in the clinical picture. That hyperthyroidism, hypothyroidism, Addison's disease, acromegaly, diabetes, gonadal conditions, and other endocrine dysfunctions often produce an untoward effect upon mental activity has been known for years.

This book by the eminent Swiss psychiatrist, who was trained in internal medicine as well as his present specialty, gives us of his own experiences and studies as well as the findings in the world literature of over 2,700 publications. It constitutes a unique type of psychiatric interpretation.

The text is presented in four parts. Part I introduces the objectives or aims, the basic principles and the limitations of the concepts. Part II is the general part dealing with the various aspects of the endocrine "psychodrom." Part III presents the psychopathology of endocrine disorders and Part IV gives the endocrinology of the psychoses and also contains a section, by Dr. R. Hess on electroencephalography applied to endocrine disorders.

The overall coverage includes the description of psychological disorders in cases of frank endocrine diseases, the explanation of the relationship between endocrine and mental phenomena when they occur in the same person and probably influence each other, and some possible therapeutic modifications of the disorders.

Regarding schizophrenia the author finds no uniform pathology for the patients. Many of them are not affected by any detectable endocrine disorders, and primary endocrine disorders are usually not accompanied by schizophrenia.

This is a remarkable book in many respects including the format, the style of presentation, the ground covered, and the excellent illustrations. The data accumulated should be of great value to the clinician and research worker. Psychiatrists, neurologists, internists, endocrinologists, and specialists in "psychosomatic" medicine will do well to have a copy.

Riese, Walter: LA PENSÉE MORALE EN MÉDICINE, Premiers Principes d'une Éthique Medicale. [Presses Universitaires de France: Pp. 84. 1954. Paper Bound. 420 Frs.]

In his *Pensée Causale en Médicine*, published in 1950 by the Presses Universitaires de France in the *Bibliothèque de Philosophie Contemporaine*, the author submitted an analysis of medical *thought* and of one of its most powerful instruments, e.i. *causal* thinking. In his *Pensée Morale en Médicine*, published in 1954 in the same series, the author endeavors to analyze the moral principles of medical *action* and to trace their history. He treats medical ethics as a particular instance of ethics at large. He defines the latter as a body of laws through which man tries to secure to his acts a most general character and scope in accordance, however, with concrete and always individual conditions and requirements.

In contrast to the conventional interpretation of medical ethics as a whole of stipulations and rules presiding over the physician's professional relations to his colleagues, the author gives priority to the physician's relation to the patient which he conceives and analyses as a human relation under special conditions. Medical ethics, he states, could not originate in primitive medicine, since here no human relation exists as yet between the two partners involved, since the sick is not conceived and addressed as an individual but solely as the residence of foreign powers, divine or evil, remaining the true target of magic treatment. Medical ethics begin with Greek or Hippocratic medicine which for the first time looked at the sick as an individual, hereby opening truly human relations between physician and patient. The principles of medical ethics are embodied in the famous Hippocratic oath, the original text of which, as well as different versions, are interpreted by the author in the light of the various civilizations in which they were conceived and formulated. The religious character of the Hippocratic oath is expressed by three factors: the invocation of the gods, the sacred community of the members, the unconditional and specific commandmants. Equipped with this basic knowledge, the reader can follow the author who analyses the ethical problems involved in the fundamental actions taken by the physician at all times; namely, interview, diagnosis, prognosis, therapy, prevention, and expertise.

The design of the book and the successfully attempted application of a workable principle of ethics to the concrete and everlasting tasks arising in medical assistance makes the volume a unique and very timely one. Repeatedly, the author discusses problems of psychological and psychopathological relevance in which ethical implications are more obvious and dramatic than in any other branch of medicine. Thus, he uncovers the moral constituent implied in the psychoanalytic conception of disease, according to which neurosis is due to a conflict between the patient's instinctive tendencies and the restrictions arising from the structure and needs of human society. The book is prefaced by the eminent French psychiatrist, Dr. Henri Baruk, Head of the well-known Charenton Hospital and Professor at the Medical Faculty of Paris.

(V. J. BIELIAUSKAS)

BOOKS RECEIVED FOR REVIEW

August, 1955

1. FARRELL, B. A. (Ed.) *Experimental Psychology, A Series of Broadcast Talks.* Philosophical Library, New York, N. Y.
2. FAUST, CLEMENS. *Die Zerebralen Herdstorungen Bei Hinterhauptsverletzungen und Ihre Beurteilung.* George Thieme Verlag, Stuttgart, Germany.
3. GLEES, PAUL. *Neurologia, Morphology and Function.* Charles C Thomas, Publisher, Springfield, Ill.
4. HUTCHINSON, BERTRAM. *Old People in a Modern Australian Community.* Melbourne University Press, New York, N. Y.; Cambridge University Press, New York, N. Y.
5. JONES, ERNEST. *The Life and Work of Sigmund Freud, Volume II, Years of Maturity.* Basic Books, Inc., New York, N. Y.
6. JOSIAH MACY, JR. Foundation, The. *The Josiah Macy, Jr. Foundation 1930–1955, A Review of Activities.* The Josiah Macy, Jr. Foundation, New York, N. Y.
7. MISIAK, HENRYK AND STAUDT, VIRGINIA M. *Catholics in Psychology.* McGraw-Hill Book Co., Inc., New York, N. Y.
8. National Research Council. *A Survey Report on Human Factors in Undersea Warfare and Supplement.* National Research Council, Committee on Undersea Warfare, Washington, D. C.
9. REED, SHELDON C. *Counseling in Medical Genetics.* W. B. Saunders Co., Philadelphia, Pa.
10. VALENTINE, C. W. *Parents and Children.* Philosophical Library, Inc., New York, N. Y.

NOTES AND NEWS

STUDY OF THERAPY PROGRAMS IN MENTAL HOSPITALS

For the first time in medical history, Veterans Administration will make an extensive evaluation of mental patient care to determine what types of treatment and hospitals best promote the improvement or recovery of its psychiatric patients and the relative costs.

VA, which has one of the nation's largest psychiatric patient loads under a single medical management, said the preliminary phases of the pioneering project have been started.

The study will continue for five years, with probably 15 of VA's 40 neuropsychiatric hospitals participating, according to Dr. Jesse F. Casey, director of psychiatry and neurology service.

Dr. Casey said the information to be sought is not now available from any source. When it is completed, he said, it should go a long way toward establishing psychiatric care on a much higher level of effectiveness and thereby speed the recovery or improvement of psychiatric patients at the least possible cost.

Dr. Casey explained that psychiatry still is virtually in its infancy. As a result, he said, the various treatment programs and types of hospitals in use today have been developed primarily on the basis of professional opinions which admittedly are not in perfect accord at this time. He said "When we complete our study, we expect to have for the first time the solid factual information we need to guide us in developing the type of hospital programs which will provide the most effective treatment for the recovery or improvement of our psychiatric patients."

The VA study, has three purposes: (1) to determine the relative effectiveness of different treatment techniques; (2) to determine the relative effectiveness of different hospital designs, staffing patterns, and program emphases, and (3) to permit valid estimates of the relative costs of the various elements in effective treatment programs.

PSYCHIATRIC CASE SEMINARS AT U.C.L.A.

Open to qualified practicing psychiatrists who are graduates of approved medical schools, an advanced Psychiatric Case seminar will meet on Wednesdays from 8 to 10 p.m. from February 1 through March 21 in room 108, Old Religious Conference Building at U.C.L.A.

Requests for application or information concerning the University of California Extension course should be made to Thomas H. Sternberg, M.D., Assistant Dean for Postgraduate Medical Education, University of California Medical Center, Los Angeles 24. Fee for the course, which is limited to twenty students, is $60.

Instructional staff members for the course are chairman, Charles W. Tidd, M.D., Professor of Psychiatry and Allen J. Enelow, M.D., Clinical Instructor in Psychiatry, both of the U.C.L.A. School of Medicine faculty.

PORTRAIT PRESENTED TO N. Y. PSYCHIATRIC INSTITUTE

On the afternoon of Thursday, October 27, an oil portrait by Soss Melik of Dr. Nolan D. C. Lewis was presented by Commissioner Paul Hoch to the New York State Psychiatric Institute in the name of the Department of Mental Hygiene of the State of New York.

Dr. Lewis was for 17 years, until his retirement in 1953, Director of the Psychiatric Institute and Professor of Psychiatry of the College of Physicians and Surgeons.

The staff and employees of the Institute, the Directors of the hospitals of the New York State Department of Mental Hygiene, and the members of the Department of Psychiatry of Columbia University were invited to be present at the reception held in Dr. Lewis' honor and for the presentation of the portrait.

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